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ENVIRONMENT AND WATER RESOURCES

WATER QUALITY GUIDELINES FOR DIISOPROPANOLAMINE (DIPA)

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EXECUTIVE SUMMARY

Introduction

Diisopropanolamine (DIPA) is an organic chemical used for a wide variety of commercial, industrial, and household applications. The primary uses of DIPA include natural gas processing, cosmetics, detergents, and corrosion inhibition. Environmental quality guidelines have not been developed for DIPA by federal or provincial agencies in Canada.

This report presents water quality guidelines for DIPA for the province of British Columbia. This work was completed by Komex International Ltd. under contract # WMB 02-060 (the "Contract") to the British Columbia Ministry of Water, Land and Air Protection, Water Management Branch. The guidelines were developed using protocols published by the Canadian Council of Ministers of the Environment (CCME), where applicable, referred to herein as "the Protocol". The guidelines are numerical limits for contaminants in water intended to maintain, improve, or protect environmental quality and human health. Water quality guidelines were developed for freshwater aquatic life, irrigation, livestock watering, and source water for drinking.

Diisopropanolamine Water Quality Guidelines

DIPA is a white solid at room temperature with a mild ammoniacal odour. It is hygroscopic, completely miscible in water, and a polar, basic solvent. DIPA has a wide variety of commercial, industrial, and household applications. Based on its physical and chemical properties, DIPA applications include gas treating, cosmetics and personal care products, detergents, metalworking fluids, coatings, corrosion inhibitors, and cement applications. DIPA sorbs strongly to the clay mineral montmorillonite, and hence its mobility in the subsurface is highly dependent on the amount and type of clay minerals in the aquifer. Biodegradation of DIPA under typical aquifer conditions can be very slow. An extensive review of existing and new toxicity studies in mammals, and vertebrates, invertebrates and plants from aquatic and terrestrial environments was undertaken to assess the toxicity of DIPA to various biota.

Water quality guidelines for DIPA were calculated, using the Protocol, for four water uses: source water for drinking, freshwater aquatic life, irrigation, and livestock watering. The recommended guidelines are summarized in Table 3.1 of this report.

Source Water for Drinking

Interim source water for drinking guidelines were calculated for children (21 mg L^{-1}) and adults (37 mg L^{-1}). The guideline protective of children is recommended.

Freshwater Aquatic Life

The Interim guideline for freshwater aquatic life was calculated to be 1.6 mg L^{-1}.

Marine Life

A guideline for marine life could not be calculated due to insufficient data quality and data quantity.

Irrigation

Four Interim guidelines were calculated for irrigation. Based on the Protocol, guidelines were calculated for 1) cereals, tame hays, and pasture crops, and 2) other crops. For each of these two groups of plants, guidelines were calculated for two soil types: 1) loam and 2) the soil that gave the most sensitive response from any plant in the toxicity testing ("poor soil"). The guidelines for cereals, tame hays, and pasture crops were 91 mg L^{-1} (loam), and 78 mg L^{-1} (poor soil). For other crops the irrigation guidelines were calculated to be 36 mg L^{-1} (loam), and 3.9 mg L^{-1} (poor soil).

Livestock Watering

Preliminary guidelines for livestock watering were calculated for dairy cattle, beef cattle, and deer, to represent likely agricultural and wild animals. The most sensitive species was the dairy cow, for which a guideline of 38 mg L^{-1} was calculated. It should be noted that these guidelines were based on studies on laboratory animals using appropriate safety factors, and no toxicological information was available for livestock species (either mammalian or avian). Should such data become available in the future, this guideline could be refined.

Data Gaps

Data gaps were identified in the toxicological dataset for DIPA, and are discussed in the main text. Overall the data gaps for this compound are relatively minor, and it is felt that the presently available toxicological dataset and the guidelines presented in this document provide a consistent picture of the toxicity of this compound.

1. INTRODUCTION

This report presents water quality guidelines for diisopropanolamine (DIPA) for the province of British Columbia. This work was completed by Komex International Ltd. (Komex) under contract # WMB 02-060 ("the Contract") to the British Columbia Ministry of Water, Land and Air Protection Water Management Branch.

1.1 Scope of Work

The scope of work for this document included the following tasks:

- review and summarize relevant available background information on DIPA;
- review and summarize the environmental fate and behaviour of DIPA;
- review and summarize available information on the toxicity of DIPA;
- conduct additional toxicity testing on four species of plant and one species of terrestrial invertebrate (Scientific Information Services (SIS));
- develop tolerable daily intakes (TDIs) of DIPA for humans and livestock (CanTox Inc.);
- derive water quality guidelines for DIPA using applicable (CCME) protocols for freshwater aquatic life, irrigation, livestock watering, and source water for drinking.

1.2 Background

DIPA is an organic chemical used for a wide variety of industrial purposes. Synthesis of DIPA was first reported in the 19th century (Siersch, 1868; Van der Zande, 1889). DIPA is not known to occur in nature. DIPA has a wide variety of commercial, industrial, and household applications. The primary uses of DIPA include natural gas processing, cosmetics, detergents, and corrosion inhibition. Environmental quality guidelines have not been developed for DIPA by federal or provincial agencies in Canada.

1.3 Protocols

Environmental quality guidelines for DIPA were developed using the following protocols developed by CCME:

A Protocol for the Derivation of Water Quality Guidelines for the Protection of Aquatic Life. (CCME, 1999).

Protocols for Deriving Water Quality Guidelines for the Protection of Agricultural Water Uses. (CCME, 1999).

For ease of reference in this document, the phrase "the Protocol" refers to whichever of the above documents is applicable. For instance, in the section on developing freshwater aquatic life guidelines, "the Protocol" would refer to CCME (1999) *A Protocol for the Derivation of Water Quality Guidelines for the Protection of Aquatic Life.* Note the Aquatic Life, and Agricultural Water Uses Protocols listed above were originally published as CCME (1991), and CCME (1993), respectively, and were reproduced with minor changes in CCME (1999).

Source water for drinking guidelines were developed using standard risk assessment algorithms and protocols (US EPA, 1989; CCME, 1996).

1.4 Toxicity Data

An extensive literature search was conducted to identify toxicity data for DIPA to mammals, and aquatic, terrestrial, and microbial organisms. Critical data gaps were identified, and two pieces of work were commissioned. 1) DIPA toxicological testing of earthworms and four plant species in four soil types was undertaken by Scientific Information Services (SIS). 2) A comprehensive review of mammalian toxicology studies for DIPA, and derivation of tolerable daily intakes (TDIs) was undertaken by Cantox Inc. (Cantox). As a result of data gaps identified in the Cantox report, a subchronic study of the oral toxicity of DIPA to rats was commissioned.

2. BACKGROUND INFORMATION

2.1 Physical and Chemical Properties

DIPA [CAS#110-97-4], $C_6H_{15}NO_2$, is known under a variety of synonyms and trade names (Table 2.1).

DIPA belongs to the group of alkanolamines. Alkanolamines are organic derivatives of ammonia and are classified based on the number of substituent groups attached to the nitrogen atom. Substitution of one organic alcohol group, ROH, for one of the hydrogen atoms of ammonia (NH_3) forms a primary alkanolamine ($ROHNH_2$). Similarly, substitution of two and three organic groups yield secondary $(ROH)_2NH$ and tertiary $(ROH)_3N$ alkanolamines, respectively (Solomons and Graham, 1988). DIPA is a secondary alkanolamine. The synthesis of DIPA was first reported in the chemical literature in the late 19th century (Siersch, 1868; Van der Zande, 1889).

Published physical and chemical properties of DIPA are summarized in Table 2.2. At room temperature, DIPA is a white solid. Alkanolamines, including DIPA, have a basicity similar to

aqueous ammonia, are completely miscible in water, and are polar solvents. They are characterized by a mild ammoniacal odour and are extremely hygroscopic. The subgroup of isopropanolamines results from the reaction of propylene oxide (C_3H_6O) with ammonia and comprises monoisopropanolamine (MIPA), diisopropanolamine (DIPA), and triisopropanolamine (TIPA), with the general formula $NH_{3-n}(CH_2CHOHCH_2CH_3)_n$.

2.2 Analytical Methods

There are currently no recommended methods for DIPA analysis published by CCME or US EPA. Generally, DIPA can be analyzed by gas chromatography, high performance liquid chromatography (HPLC), ion chromatography (IC), or wet test methods (Kirk-Othmer, 1999).

Methods using derivatization, gas chromatograph (GC) separation, and flame ionization detection (FID) were described by Bachelor (1976) and Langvardt and Melcher (1980). GC methods without derivatization using packed or capillary columns were reported by Salanitro and Langston (1988) using direct injection and a nitrogen-phosphate detector and Dawodu and Meisen (1993) using a flame ionization detector.

GC methods for DIPA analysis were summarized by Witzaney and Fedorak (1996) and evaluated by CAPP (1997). Direct injection using a flame ionization or nitrogen-selective detector in combination with a capillary column did not yield satisfactory results. Problems were attributed to contamination of the injection port liner. Similarly, DIPA analysis using a packed stainless steel column and a flame ionization detector was associated with carryover ("ghosting") and required that the column was conditioned. DIPA analysis using a non-polar, megabore, thick-filmed capillary column which had been base-deactivated and using a nitrogen-selective detector were more successful. However, the matrix of the samples studied contained NH_4Cl and chloroform, which interfered with the nitrogen-selective detector.

Methods for DIPA analysis employing high performance liquid chromatography were discussed by Einarsson *et al.* (1986), Nasholm *et al.* (1987), and Serbin and Birkholz (1995).

Headley *et al.* (1999) described a method for analysis of vegetation samples collected from a DIPA-contaminated wetland. Sample preparation included grinding and homogenizing frozen vegetation samples under liquid nitrogen. Ground samples were transferred into centrifuge tubes and allowed to warm to room temperature. Following addition of deionized water and equilibration for 45 minutes, samples were centrifuged for 45 minutes at 2,500 rpm. DIPA supernatants were analyzed using ion chromatography-electrospray ionization-tandem mass spectrometry.

Analytical methods used by two commercial laboratories that routinely conduct environmental DIPA analysis of water and soil samples are summarized below:

The first laboratory performs DIPA analysis based on the method described by Einarsson *et al.* (1986) and Serbin and Birkholz (1995). Water samples or aqueous extracts of soil samples are derivatized to 9-fluorenylmethyl formides. Analysis is then performed by HPLC. Detection limits are 1 mg L^{-1} and 2.5 mg kg^{-1} for water and soil, respectively.

The second laboratory uses an IC method for DIPA analysis. Water samples are filtered prior to analysis. Soil samples are extracted with deionized water and the extract is also filtered. Water samples or extracts are analyzed by IC using a specialized column for separation and a two-solvent gradient. DIPA detection is achieved with an electrochemical detector using pulsed amperometry. Detection limits are 0.005 mg L^{-1} and 0.05 to 0.1 mg kg^{-1} for water and soil, respectively.

2.3 Production and Uses

2.3.1 Production

Isopropanolamines have been commercially available for over 40 years (Kirk-Othmer, 1999). DIPA is synthesized by a reaction of propylene oxide (C_3H_6O) with ammonia (NH_3). The reaction path is shown below:

$$2C_3H_6O + NH_3 \rightarrow C_6H_{15}NO_2$$

In North America, the Dow Chemical Company (Dow) is the dominant DIPA producer. In 1995, the US production was estimated by Dow to be approximately 7,000 tons per year (approximately 3,200 L). Commercially, DIPA is available as commercial grade compound (98% pure, containing a maximum of 0.5% water) and as low freezing grade DIPA (containing 10 or 15% (wt.) deionized water).

2.3.2 Uses

DIPA has a wide variety of commercial, industrial, and household applications. Based on its physical and chemical properties, DIPA applications include gas treating, cosmetics and personal care products, detergents, metalworking fluids, coatings, corrosion inhibitors, and cement applications. Commercial and industrial uses of DIPA summarized by Dow (1999) and Kirk-Othmer (1999) are provided below.

2.3.2.1 Gas Treating

DIPA is used as solvent in the Sulfinol process to remove acid gases from natural gas streams. The Sulfinol process was introduced by Shell in 1963 and consists of passing the natural sour gas stream through a mixture of sulfolane, DIPA, or methyldiethanolamine, and water (*e.g.*, Dunn, 1964; Fisch, 1977; Yogish, 1990; MacGregor and Mather, 1991; Murrieta-Guevarra *et al.*, 1994). Acid gases including hydrogen sulphide (H_2S), carbon dioxide (CO_2), carbonyl sulphide (COS), carbon disulphide (CS_2), and mercaptans (thiols) are physically absorbed by sulfolane and chemically absorbed by DIPA thereby "sweetening" the gas stream.

DIPA is also used in alkanolamine-based acid gas removal (AGR) or "sweetening" processes (Sorensen *et al.*, 1996). In the AGR process, the weakly basic alkanolamines react with acid gases to form salts that are thereby removed from the gas stream. Amine salts are subsequently decomposed by thermal regeneration. DIPA is used in gas sweetening processes based on an H_2S selectivity (Goar and Arrington, 1979).

2.3.2.2 Cosmetics and Personal Care Products

Alkanolamine salts, including DIPA salts, are used as raw materials in the manufacture of creams (Jellinke, 1970; Balsam and Sagarin, 1972; Navarre, 1975), lotions, shampoos, soaps, and cosmetics based on their high foaming properties and low skin irritation. DIPA and MIPA may comprise up to 10% of emulsifying agents for cosmetic lotions, bath preparations, and neutralizers in cosmetics (Beyer *et al.*, 1987). Chemistry similar to that used in soluble oils and other emulsifiers is applicable to cleansing creams and lotions (Otomo *et al.*, 1989; Sukai *et al.*, 1989). Isopropanolamines, including DIPA, neutralize acidic components, and provide a balanced pH and suitable surfactant properties for hair sprays, hair wave lotions, skin lotions, and moisturizers.

2.3.2.3 Detergents and Cleaners

DIPA is used extensively in soaps, cleaning products, and detergents as an emulsifying and wetting agent, a foam stabilizer, and a rinse improver (Dow, 1999). Alkanolamines (including DIPA) are also used in phosphate-free liquid detergents (Kirk-Othmer, 1999). In non-enzyme products, they contribute alkalinity, pH control, and enhancement of product stability. In enzyme products, alkanolamines contribute to the stability of the enzyme in water solutions (*e.g.*, Hughes, 1985).

2.3.2.4 Metal Working Fluids

Isopropanolamines (DIPA, MIPA, and TIPA) are widely used in the metal working industry for corrosion protection, lubrication, foam suppression, and reduction of friction in metal cutting operations.

2.3.2.5 Coatings

In metal-coating preparations, alkanolamines (including DIPA) are used as metal-complexing agents, neutralizers, promoters, modifiers, corrosion inhibitors (Brangs and Heinrich, 1969), and in electrocoating (Wehrmann, 1972; Obana and Miyagawa, 1979). DIPA further assists in improving curing resins, improving storage stability, and improving both fresh and salt water resistance for some types of coatings (*e.g.*, Takahashi *et al.*, 1974; Vassiliou, 1976; Butler, 1978). In water-borne coatings, DIPA is used for acid neutralization, improvement of water solubility, and reduction of water sensitivity and discoloration (Dow, 1999).

2.3.2.6 Corrosion Inhibitors

Alkanolamines (including DIPA) inhibit corrosion of ferrous metals (Brangs and Heinrich, 1969). Applications include coolant systems, lubricating oils (Stanik *et al.*, 1988; De Jong *et al.*, 1989), metal working fluids, petroleum anti-fouling (Forester, 1989), and drilling needs (Mukhin *et al.*, 1989). Corrosion inhibitors for aluminum that contain alkanolamines have also been discussed in the literature (Imai *et al.*, 1988).

2.3.2.7 Cement Applications

Among other alkanolamines (*e.g.*, MIPA and TIPA), DIPA is often used in cement admixtures as an accelerator to reduce set time (Kobayashi and Fukazawa, 1989; Dow, 1999).

2.3.2.8 Miscellaneous Uses

Additional applications for DIPA include herbicides, pesticides, insecticides, paint strippers, wax removers, polishes, paper and paperboard, photographic intermediates, plastics and polymers, and as polyurethane additive.

2.4 Levels in the Canadian Environment

The occurrence of DIPA in the environment has been reported in groundwater, surface water, soil, and plants in the vicinity of facilities where it has been used. It is anticipated, however, that in environments located away from such facilities (*i.e.*, most of Canada), DIPA will not be present at measurable concentrations.

Reports on the presence of anthropogenic DIPA in the environment are limited to data collected at three sour gas processing facilities in Alberta and British Columbia (CAPP, 1997; Wrubleski and Drury, 1997). At these facilities, a maximum soil DIPA concentration of 1,480 mg kg^{-1} was measured in clay-rich till. Maximum measured DIPA concentrations in groundwater collected from contaminated aquifers beneath the gas processing facilities were 6 mg L^{-1} in a sand aquifer and 590 mg L^{-1} in a shallow till aquifer (Greene *et al.*, 1999). At one of the facilities, DIPA-impacted groundwater discharged via a wetland into a creek. Levels within the wetland and the creek were significantly reduced compared to the discharging groundwater. Maximum DIPA concentrations reported in groundwater and creek water were 590 and 0.07 mg L^{-1}, respectively (Greene *et al.*, 1999).

DIPA uptake by wetland vegetation was studied as part of a CAPP research program to evaluate natural attenuation processes in contaminated wetlands (CAPP, 1998; 1999; 2000). Roots, stems, leaves, flower heads, seed heads, and berries of cattail, dogwood, sedge, marsh reed grass, cow parsnip, and smooth brome growing in a DIPA-impacted wetland were included in the study (CAPP, 1999 and 2000; Headley *et al.*, 1999). Analytical results indicated highly variable DIPA concentrations for different parts of the same species (*e.g.*, roots versus leaves), between different plant species (*e.g.*, cattail leaves versus sedge leaves), and even between different samples of the same part of the same species. The maximum measured DIPA concentration in plants from the wetland was 208 mg kg^{-1}. The maximum measured DIPA concentration in water within the wetland was 13 mg L^{-1}.

No studies were found that had detected DIPA as naturally-occurring compound in the environment.

2.5 Existing Guidelines and Criteria in Various Media

Federal or provincial environmental quality guidelines have not been developed for DIPA.

2.6 Environmental Fate and Behavior

The fate and behavior of a compound released to the subsurface environment is determined by the physical and chemical properties of the compound and the attenuation processes (*e.g.*, biodegradation) to which it is subjected. The relationship between compound properties, and fate and behavior can be used to predict the potential for the persistence and transport of DIPA. Physical and chemical properties of DIPA (Table 2.2) in combination with recently published sorption studies and an alkanolamine fate and transport study conducted by Sorensen *et al.*

(1996) are discussed in the sections below to evaluate the environmental fate and behavior of DIPA.

The environmental fate and behavior of DIPA is affected by its physical and chemical properties and susceptibility to biodegradation, as well as the hydrogeological and geological properties of the aquifer material.

2.6.1 Adsorption and Mobility

Luther *et al.* (1998) investigated DIPA sorption parameters in batch equilibration studies. Sorbent materials included aquifer sediments from DIPA-contaminated sour gas treatment facilities, reference soils of pure montmorillonite and kaolinite, and six soils of various clay and organic matter contents. DIPA sorption isotherms were found to be curvilinear, and the slope decreased with increasing concentration. X-ray analysis of DIPA-saturated montmorillonite showed that DIPA enters the interlayer space of the mineral. Sorption by aquifer materials was interpreted to be relatively independent of organic carbon content, but a strong function of montmorillonite content. The DIPA distribution coefficient (K_d) for montmorillonite (16 to 42 L kg^{-1}) was higher than for humus-rich soil (2.0 L kg^{-1}). Cation exchange capacity (CEC) was found to be a reasonable predictor of DIPA sorption by soils and aquifer materials with low organic carbon content (*i.e.*, <1%).

DIPA retardation coefficients calculated by Luther *et al.* (1998) for aquifer sediments were reported to be 3.2 (weathered sandstone), 5.3 (weathered shale/sandstone), and 12 (clay-rich till). These values indicate that, particularly in the presence of clay-rich sediments, DIPA migration is significantly retarded relative to groundwater flow velocity.

The organic carbon-water partition coefficient (K_{oc}) and the *n*-octanol-water partition coefficient (K_{ow}) represent the equilibrium ratio of DIPA sorbed by organic carbon or octanol to its concentration in water, respectively. The low K_{oc}, low K_{ow}, pKa (negative logarithm of the acid dissociation constant), and high water solubility of DIPA (Table 2.2) are consistent with the findings of the sorption study, summarized above, that there is a low potential for DIPA to sorb to sediments or soils, unless montmorillonite-rich clay comprises a significant fraction of aquifer sediments.

2.6.2 Aqueous-Phase Solubility

DIPA is highly water soluble and considered miscible at 25° C (Verschueren, 1996; Kirk-Othmer, 1999). Its pKa of 8.9 indicates that DIPA exists in an increasingly protonated form at pH values less than 8.9, and acts as a weak base in water (Kim *et al.*, 1987).

2.6.3 Leaching and Lateral Movement

The leaching and lateral movement potential of DIPA is determined by its relatively strong affinity for sorption to montmorillonite, low retardation coefficients in DIPA-contaminated aquifer sediments (except for montmorillonite), and high solubility. CAPP (1997) used the classification system of McCall *et al.* (1980) to classify DIPA mobility as very high to medium. The mean retardation factor estimated from the data for DIPA at three sour gas facilities was 6.8 (Luther *et al.*, 1998). Thus, DIPA is predicted to partition between water and montmorillonite in the vadose (*i.e.*, unsaturated) zone. Once in the saturated zone, the migration rate of DIPA is a function of the clay content (*i.e.*, montmorillonite) of the aquifer material, the hydraulic conductivity of the aquifer material, the hydraulic gradient, and the susceptibility of DIPA to biological attenuation processes (*i.e.*, biodegradation).

2.6.4 Biodegradation

The biodegradation of DIPA has been investigated in acclimated sewage sludge, refinery wastewater, laboratory microcosm studies using contaminated aquifer sediments, and as part of a natural attenuation study in natural wetlands. Most studies have demonstrated that DIPA biodegrades in aerobic microcosms from a variety of DIPA-contaminated environmental samples. Reported DIPA biodegradation rates and lag times (*i.e.*, time required before degradation starts) are highly variable. Biodegradation rates range from 0 to 70 mg L^{-1} day^{-1}. Lag times range from <1 to 220 days (Table 2.3).

Witzaney and Fedorak (1996) reviewed previous work conducted on DIPA biodegradation. The review indicated that some studies provided evidence of DIPA degradation (Bridié *et al.*, 1979a; Salanitro and Langston, 1988; Chong, 1994), whereas results of Rothkopf and Bartha (1984) suggested that DIPA did not support microbial growth.

In recent studies, DIPA biodegradation using nutrient-amended and -unamended microcosms, under aerobic and anaerobic conditions, and at temperatures ranging from 8° to 28° C has been examined. Microcosm studies were conducted using sediments and soils from DIPA-contaminated aquifers. Microcosm materials included sandstone, till, sand, and wetland sediments. Materials, conditions, lag-times, and biodegradation rates reported in microcosm studies are summarized in Table 2.3.

Gieg *et al.* (1998) conducted aerobic and anaerobic microcosm studies at 8° and 28° C using a variety of sediments from contaminated aquifers. Shake flask cultures were incubated at 8° and 28° C under addition of the appropriate nutrients such as nitrogen and phosphate. This study

documented the presence of aerobic and anaerobic microbial DIPA degraders in contaminated aquifer sediments from three sour gas treatment facilities. Under aerobic conditions at 28° C, DIPA was completely removed. DIPA removal was significantly slower at 8° C and complete DIPA removal was not achieved. Refeeding of microcosms with additional DIPA led to faster and complete DIPA removal at 8° and 28° C. Kinetic analyses indicated that DIPA degradation is best described by first-order kinetics. Under anaerobic conditions, DIPA biodegradation was confirmed to occur at 28° C under NO_3^-, Mn^{4+}, and Fe^{3+} reducing conditions. At 8° C, evidence of anaerobic degradation under NO_3^-, Mn^{4+}, and Fe^{3+} reducing conditions was observed in a limited number of microcosms.

Gieg *et al.* (1999) used radio-labelled ^{14}C-DIPA to investigate the microbial mineralization of DIPA. They demonstrated the release of $^{14}CO_2$ from ^{14}C-DIPA and the reduction of the respective electron acceptors in aerobic and anaerobic microcosm studies at 8° and 28° C. In anaerobic cultures, DIPA degradation was observed under NO_3^- and Mn^{4+} reducing conditions at 8° and 28° C, whereas DIPA-degrading activity was difficult to sustain under Fe^{3+} reducing conditions. In aerobic cultures, between 30 and 50% of the nitrogen from DIPA was found as ammonium-nitrogen.

West (1995) suggested that the DIPA biodegradation pathway occurs via the metabolites N-(2-oxopropyl)-isopropanolamine to MIPA and methylglyoxal. MIPA has been identified as an intermediate metabolite in soil microcosms (CAPP, 1997). The aerobic microbial metabolism of MIPA was studied by Jones and Turner (1973). The aerobic pathway occurred via initial activation to 1-aminopropan-2-ol O-phosphate to propionaldehyde, which was subsequently oxidized to propanoic acid. Propanoic acid was hypothesized to be further metabolized. Anaerobic biodegradation of MIPA was investigated by Chou *et al.* (1978), who documented that MIPA can be biodegraded under methanogenic conditions.

2.6.5 Volatilization

Volatilization potential is commonly expressed using the Henry's law constant and the vapour pressure of a compound. The Henry's law constant is the equilibrium ratio of the concentration in the gas phase to the concentration in the aqueous phase. This value is closely related to the vapour pressure of a compound but is also dependent on its aqueous solubility and molecular weight and, therefore, can be used to make a more accurate prediction of volatility than one based on solely on vapour pressure.

Lyman *et al.* (1982) used Henry's law constants to classify volatilization potential as follows:

- values less than 10^{-7} atm m^3 mol^{-1} indicate that the substance is less volatile than water and can be considered essentially non-volatile;
- values between 10^{-7} and 10^{-5} atm m^3 mol^{-1} indicate that the substance may volatilize slowly but the compound will still tend to partition into the aqueous phase;
- values between 10^{-5} and 10^{-3} atm m^3 mol^{-1} indicate that volatilization is significant; and,
- values greater than 10^{-3} atm m^3 mol^{-1} indicate that the majority of the mass of the compound will tend to partition into the gas phase.

The vapour pressure of a compound is the pressure that the vapour phase of a compound exerts at equilibrium with its aqueous phase. Vapour pressures are reported for a given temperature and increase with increasing temperature. Compounds with high vapour pressures are more likely to volatilize than those with lower vapour pressures. Thus, the potential of vapour-phase transport of a compound increases with increasing vapour pressures.

The low Henry's law constant of DIPA (1.72×10^{-7} atm m^3 mol^{-1}), combined with a low vapour pressure (*i.e.*, 0.02 mm Hg at 41°C) (Table 2.2), suggest that DIPA can be considered essentially non-volatile. Thus, vapour-phase transport in the vadose zone is not expected to be significant.

2.6.6 Photolysis

No information on the susceptibility of DIPA to phototransformation reactions was available at the time this report was prepared.

2.7 Behavior and Effects in Terrestrial Biota

2.7.1 Terrestrial Plants

The toxicity of DIPA to terrestrial plants is summarized in Table 2.4. Two toxicity studies have been completed. Data for both studies is provided in CAPP (2001).

The first study (Komex, 1999) conducted on lettuce (*Lactuca sativa)*, consisted of a five day seed germination/root elongation test. This is a widely-used and accepted short-term test for plants (*e.g.*, Ratsch and Johndro, 1986; Wang, 1987; Wang and Williams, 1988; ASTM, 1990). For lettuce (*Lactuca sativa*) grown in a fine-textured soil, Komex (1999) reported NOEC values of 140 and 6,300 mg kg^{-1}, for root elongation and seed germination, respectively (Table 2.4).

The second plant toxicity study (CAPP, 2001), was conducted using an Environment Canada (1998) draft protocol, four plant species (lettuce (*Lactuca sativa),* carrot *(Daucus carota),* alfalfa *(Medicago sativa),* and timothy (*Phleum pratense*)), and four soils with differing texture, organic

carbon content, and cation exchange capacity. The endpoints measured were emergence, biomass, root length, and shoot length (Table 2.4). For all four plant species, the most sensitive endpoint was root length. The lowest LOEC for this endpoint was 424 mg kg^{-1} (lettuce and carrot in sand). The highest LOEC was 43,700 mg kg^{-1} for timothy emergence in loam. Plants were generally most sensitive in sand and least sensitive in loam.

2.8 Behavior and Effects in Aquatic Biota

Available data on the toxicity of DIPA to freshwater and marine aquatic species are presented in Table 3.6. Toxicological studies on rainbow trout (*Oncorhynchus mykiss*) and the sideswimmer (*Hyalella azteca*) were commissioned for this report. A full report on this work is included in CAPP (2001). Note that ERAC (1998) included a review of previous published and unpublished freshwater aquatic toxicological data, and a report on freshwater toxicological studies, which were commissioned for the ERAC (1998) report. References to ERAC (1998) in the following sections refer only to the new data commissioned for the report. Original references are used for other studies referenced in the ERAC (1998) report.

DIPA has a pKa of 8.9 (Table 2.2), which means that below a pH of 8.9, DIPA is present predominantly in its charged, protonated form. Conversely, above pH 8.9, DIPA is predominantly unprotonated (Section 2.6.2). This behaviour has the potential to affect DIPA's toxicity to freshwater aquatic life. Moreover, adding DIPA to water with a low buffering capacity will result in an alkaline pH, which may preclude the survival of certain organisms, due to pH alone. Accordingly, pH was included in Table 2.5, where available.

2.8.1 Freshwater Aquatic Life

2.8.1.1 Aquatic Vertebrates

Data were available for seven species of aquatic vertebrates (Table 2.5). An acute lethality study on rainbow trout (*Oncorhynchus mykiss*) was completed for CAPP (2001). ERAC (1998) completed a 7 day survival and growth test on fathead minnows (*Pimephales promelas*). The results of acute lethality studies on clawed toad (*Xenopus laevis*), goldfish (*Carassius auratus*), ide (*Leuciscus idus*), mosquito fish (*Gambusia sp.*), and stickleback (species not specified) were also available. Reported LC_{50} values for the acute tests ranged from 42 mg L^{-1} (stickleback) to 7,698 mg L^{-1} (rainbow trout). The LOEC for the 7 day growth endpoint for the fathead minnow was 1,000 mg L^{-1} at both test pHs.

2.8.1.2 Aquatic Invertebrates

Four studies considered the toxicity of DIPA to three species of aquatic invertebrates (Table 2.5). An acute lethality study on a sideswimmer (*Hyalella azteca*) was completed at two pH values (CAPP, 2001). Two studies reported the acute lethality of DIPA to *Daphnia magna*, and one study investigated the 7 day reproduction and survival endpoints in *Ceriodaphnia dubia*. Reported LC_{50} values for the acute tests ranged from 278 mg L^{-1} (*D. magna*) to 1,128 mg L^{-1} (*H. azteca*, pH 7.5). The LOECs for the non-lethal (reproduction) endpoints for *C. dubia* were 31 mg L^{-1} at the lower pH (7.7 to 8.4) and 250 mg L^{-1} at the higher pH (8.2 to 9.4).

2.8.1.3 Aquatic Plants

Only one study for an aquatic vascular plant was available. SRC (1994) reported the EC_{50} for duckweed (*Lemna minor*) growth to be 1,500 to 2,300 mg L^{-1}. Two studies on the green alga *Selenastrum capricornutum* and one study on the green alga *Scenedesmus suspicatius* were available for various endpoints. The EC_{50}/LC_{50} values ranged from 7 mg L^{-1} to 270 mg L^{-1}.

2.8.1.4 Other Aquatic Biota

Other aquatic biota include all aquatic organisms not included in the animal or plant kingdoms. This covers organisms from the kingdoms Monera, Protista, and Fungi. A study by SRC (1994) measured ^{14}C uptake and nitrogen fixation by the cyanobacteria *Aphanizomenon flos-aquae* and ^{14}C uptake by the diatom *Cyclotella meneghiana*. The reported EC_{50} values ranged from 110 mg L^{-1} to 200 mg L^{-1}.

2.8.2 Marine Life

2.8.2.1 Marine Vertebrates

Literature data were not available for marine vertebrates

2.8.2.2 Marine Invertebrates

Literature data were not available for marine invertebrates

2.8.2.3 Marine Plants

Literature data were not available for marine plants

2.8.2.4 Other Marine Biota

Other marine biota include all marine organisms not included in the animal or plant kingdoms. This covers organisms from the kingdoms Monera, Protista, and Fungi. Two studies examined the effect of DIPA on the luminescence of the marine bacterium *Vibrio fischerii* (SRC, 1994; ERAC, 1998). The reported EC_{50} values ranged from 50 to 9,202 mg L^{-1}.

2.9 Behavior and Effects in Mammalian Species and Humans

2.9.1 Mammalian Species

Literature studies on the toxic effects of DIPA to mammals are presented in Table 2.6. This section represents a summary of the review of mammalian DIPA toxicology undertaken by Cantox for the CAPP (2001) report. The complete Cantox report is available in CAPP (2001).

2.9.1.1 Acute Toxicity Studies

Animal studies summarizing the acute lethality of DIPA using single dose exposures (LD_{50}) are summarized in Table 2.6. Test animals have included rat, mouse, guinea pig, and rabbit.

Oral Studies

A 30% aqueous solution of DIPA was administered orally to two groups of rats (two animals per group). The first group received a total dose of 2,000 mg kg^{-1} bw without observable effect. A second group received a dose of 3,980 mg kg^{-1} bw, and both died within 24 hours (Dow, 1954).

The acute toxicity of two sunscreen formulations containing DIPA (1%) was determined in male and female albino rats, or Sprague Dawley rats. When administered by gavage, the LD_{50} for one of the sunscreen preparations was 5,000 mg kg^{-1} bw in one instance, but this dose was tolerated in the second study. At lower doses, there were no toxicological effects up to 14 days after treatment (Biosearch, 1981a; Springborn, 1982a).

In another study, rats given 5,000 mg kg^{-1} bw day^{-1} for seven days produced no evidence of toxic effect (BIBRA, 1991).

Dermal and Ocular Studies

There are several studies that have examined the skin irritation and dermal toxicity of DIPA. Undiluted DIPA was applied to intact, or abraded skin on the abdomens of rabbits (Dow, 1954). Moderate hyperemia to severe necrosis were observed at the intact sites, and slight hyperemia, oedema, and moderate denaturation were observed where DIPA was applied to abraded skin. A

10% aqueous solution of DIPA applied to rabbit ears had no observable effect. When applied to either normal or abraded skin on the abdomens of rabbits, however, this dose of DIPA produced moderate hyperemia and blistering, oedema, and moderate denaturation (Dow, 1954).

Undiluted DIPA is a severe eye irritant in rabbits. Application of 50 mg DIPA directly to the eye caused burns of the eyelid, eyeball and corneal mucosa (Toropkov, 1980a). Recovery occurred in 22 days, but ocular burns that produced cataracts or opaque corneas remained. A dilute solution (1% DIPA) was tested in a sunscreen formulation on New Zealand rabbits to evaluate skin irritation. The application of 0.2 mL of undiluted product produced evidence of mild primary irritation (Springborn, 1982b).

The ocular irritation produced by a sunscreen containing DIPA (1%) was evaluated in two studies in albino rabbits. Eyes were treated briefly with the solution and immediately rinsed, or were treated and then left unattended for up to seven days. The product was deemed not to be an ocular irritant (Biosearch, 1981b; Springborn, 1982c).

2.9.1.2 Subchronic Toxicity Studies

DIPA has been tested in rats for responses to subchronic exposures in drinking water. Groups of five male and five female CFD Fischer 344 rats (ten animals per dose) were given doses of 0, 100, 300, 600, 1,200, or 3,000 mg kg^{-1} bw day^{-1} in their drinking water for a period of two weeks. Observations of activity and physical characteristics were recorded during the exposure period, at the end of which animals were examined for gross pathological changes, or changes in organ weights. Histological studies were performed on liver, kidney, and urinary bladder (Dow, 1984).

The 3,000 mg kg^{-1} bw day^{-1} dose of DIPA was not well-tolerated by either sex. Two of five male rats died before the completion of the two week study. Other animals demonstrated marked weight loss, reductions in body fat, organ sizes and weights, and altered clinical biochemical parameters. These changes were partially attributed to emaciated states from marked decreases in food and water consumption. At the highest dose, rats suffered acute inflammation and degeneration of kidney and urinary bladder. There was evidence of generalized liver atrophy, but no clear evidence of hepatotoxicity (Dow, 1984).

Animals dosed at 1,200 mg kg^{-1} bw day^{-1} were observed to have lower dietary and water intake which accounted for a small weight decrease in males, but the rate of weight gain for females was unaffected. Kidney weights (relative to control animals) were slightly increased in this group. The type of kidney alterations observed in the high-dose animals was observed on histological examination of only one animal at this dose. All other rats of either sex showed no treatment related effects in any of the organs examined.

No toxicological effects were observed among animals that received 600 mg kg^{-1} bw day^{-1} or less in this study (Dow, 1984). As such, this dose rate could be considered the study no-observable-adverse-effect-level (NOAEL).

Wistar rats that received 1% DIPA mixed with their powdered diet from age 6 weeks to 24 weeks showed no evidence of renal toxicity. There was no evidence of endogenously produced *N*-nitrosobis(2-hydroxypropyl)amine detected in urine collected from these animals (detection limit 50 nmol per 200 mL) (Konishi *et al.*, 1991).

In another study, rats given 5,000 mg kg^{-1} bw day^{-1} for seven days produced no evidence of toxic effect (BIBRA, 1991). In the guinea pig, a threshold for toxic effects for less than chronic exposures was given at 0.22 mg kg^{-1} bw day^{-1} (Toropkov, 1980b).

2.9.1.3 Chronic Toxicity and Oncogenicity Studies

There was no increase in the incidence of tumors observed in target organs of Wistar rats fed 1% DIPA (w/v) for a period of 94 weeks (Yamamoto *et al.*, 1989; Konishi *et al.*, 1991). The dosage of DIPA was 391 ± 35 mg kg^{-1} bw day^{-1}.

The lung, oesophagus, urinary bladder and kidney, as well as the nasal cavity, are recognized target tissues for nitrosated diisopropanolamine. Among 16 treated rats that survived the full 94 week exposure period, there were no tumors of the nasal cavity, none in the lung, oesophagus, liver, urinary bladder, or kidney. There were also no thyroid adenomas in any of the treated animals, while one rat of 19 control animals had thyroid adenomas (Konishi *et al.*, 1991). These are sites known to be susceptible to tumor formation in rats exposed to *N*-nitrosobis(2-hydroxypropanol)-amine. In addition, the spontaneous tumor frequency in adrenal gland, testis, and pituitary gland was lower in DIPA treated animals than the controls. This indicates that chronic (lifetime) exposure to 391 ± 35 mg kg^{-1} bw day^{-1} of DIPA was not carcinogenic (Yamamoto *et al.*, 1989).

When fed a similar diet in conjunction with a source of nitrite in the drinking water (0.3% but not 0.15%), tumors appeared in every expected target organ. This was taken as evidence of endogenous production of *N*-nitrosobis(2-hydroxypropanol)amine in conditions of simultaneous exposure to DIPA and nitrite. Analysis of urine from animals chronically exposed to both substances for a period of 24 weeks also showed evidence of *N*-nitrosobis(2-hydroxy-propanol)amine from endogenous enzymatic activity. In conditions where the animals' diet had no source of excess nitrite, exposure to DIPA produced none of this carcinogenic material based on the detection limit of the assay. Animals treated with DIPA at a dose of 448 ± 36 mg kg^{-1} bw day^{-1} with a daily nitrite intake of 151 ± 16 mg kg^{-1} bw day^{-1} developed significant numbers

of tumors at all sites examined. These were similar in type and location to tumors induced by exposure to *N*-nitrosobis(2-hydroxypropanol)amine alone (Yamamoto *et al.*, 1989). Among animals that received similar doses of DIPA, but reduced nitrite (0.15% instead of 0.3% in drinking water), tumor frequency in target tissues was not significantly different from control animals. This suggests a threshold of tumor response in the rat, even though there is evidence for production of the carcinogenic substance most likely responsible for tumor production. This cannot be taken to mean that a combination of high nitrite exposure with DIPA is essential for carcinogenic initiation in tissues.

Yamamoto *et al.* (1989) suggest that their results provide evidence that endogenous nitrosations of environmental nitrosatable amines can be potential risk factors for human cancer development.

2.9.1.4 Genetic Toxicology Studies

When evaluating data for genotoxicity, primary goals are to determine (1) the likelihood of occurrence of a key event and (2) whether that event might lead to heritable changes associated with any adverse effect *in vivo*, including cancer. The basis upon which a weight-of-evidence evaluation can be constructed include the following:

- any statistically significant observations should be reproducible and biologically significant;
- a dose-response relationship should exist for effects;
- the effects should be permanent and progressive, as opposed to reversing upon cessation of chemical dosing;
- the nature of DNA effects should be characterized;
- the database should be consistent or inconsistencies adequately explained; and,
- the effects produced in the assay should be relevant to humans.

A central objective of the weight-of-evidence approach is to balance experimental test data with experience, and not to accord greater weight to any single result. For purposes of human hazard assessment, greater confidence is placed in those test systems that examine possible genetic effects from chemical exposure of animals, rather than in tests that rely on selected homogeneous cell populations raised and tested *in vitro*. Chemical exposures of biological systems carried out *in vitro* are much less realistic, and results of such tests can be determined by the effects of toxicity. Such toxicity can occur at unusually high exposure concentrations and/or be dependent on metabolic and detoxification capabilities. Finally, a weight-of-evidence evaluation seeks to establish a dose-response relationship. Greater attention should be given wherever there is a clear association between increased exposure and a genetic effect.

The consideration of the carcinogenic potential of DIPA can be assessed in a number of ways.

Short-term tests for mutation, or for other evidence of genotoxic activity, allow identification of alterations in the genome. A primary purpose of such tests is to provide information on the production of heritable changes (mutations) that could lead to further adverse biological consequences. An initial and prominent question that genotoxicity tests are designed to answer, is whether the chemical (or any derivative) interacts directly with and mutates DNA (Williams, 1989). Such interactions are known to bring about changes in gene expression or to affect other key biological processes. However, there is clear evidence that some short-term tests demonstrate effects of toxicity that may or may not support direct interaction with DNA. Finally, some chemical exposures show no effect at low dosages, and can be shown to be dependent on a threshold of exposure to produce an effect. The production of such indirect effects is often limited to conditions of high dose, which may be irrelevant to health risk assessment.

The genotoxicity of DIPA has not been extensively investigated. One study in *Salmonella* was negative (at doses up to 10 mg plate^{-1}) in several standard tester strains including TA100, TA98, TA 1535, and TA1537 with or without microsomal activation using rat or hamster liver S9 (Mortelmans *et al.*, 1986). An unpublished report (Dow, 1994) has examined DIPA in the *in vitro* chromosomal aberration test (OECD Guideline 473). The purpose of the *in vitro* chromosome aberration test is to identify agents that cause structural (chromosome or chromatid type) chromosome aberrations in cultured mammalian cells. Chromosome mutations and related events are the cause of many human genetic diseases and there is substantial evidence that chromosome mutations and related events causing alterations in oncogenes and tumor suppressor genes of somatic cells are involved in cancer induction in humans and experimental animals. DIPA did not produce chromosomal aberrations in rat lymphocytes with and without metabolic activation at exposures of 313 to 5,000 µg mL^{-1} (Dow, 1994 in BASF, 1994). There were no other published reports in the literature.

While DIPA may not be genotoxic, a related nitroso-derivative that can be produced in the environment and endogenously in certain conditions does have genotoxic potential. Commercial DIPA prepared by chemical synthesis from propylene oxide and ammonia has been reported to contain between 20 and 1,300 ppb of *N*-nitrosobis(2-hydroxypropyl)amine (Issenberg *et al.*, 1984). Older samples (>5 years storage) exhibited the highest concentration of this contaminant. Recent commercial synthetic practice (Dow, 1985a) produces product with no evidence of *N*-nitrosobis(2-hydroxypropyl)amine at a detection limit of 20 ppb. Therefore, it is likely any of this product found in the environment would be the result of biological or direct chemical reactions.

N-nitrosobis(2-hydroxypropyl)amine has genotoxic properties. It is rapidly absorbed through the skin of hamsters, and topical application produced neoplasms of the lip, cheek pouch, and vaginal epithelium (Pour *et al.*, 1977; 1980). *N*-nitrosobis(2-hydroxypropyl)amine has been

identified as a potent pancreatic carcinogen in hamsters (Pour *et al.*, 1974). Oral ingestion (drinking water) in rats, induced neoplasms of the colon, respiratory tract, esophagus, and liver (Lijinsky *et al.*, 1978; Pour *et al.*, 1979). In mice, it induced neoplasms in the lung, liver, and nasal cavity. In rabbits and guinea pigs, it induced neoplasms in the liver.

There is no evidence that DIPA is either genotoxic in short-term assays or carcinogenic in a 94 week bioassay conducted in Wistar rats. DIPA, therefore, does not pose a genetic hazard as a result of exposure. There is, on the other hand, ample evidence that DIPA may undergo nitrosation reactions either in the environment, or after ingestion by endogenous mechanisms, when sources of nitrite are available. Since DIPA undergoes biodegradation in the environment primarily by oxidative metabolism, DIPA from groundwater sources would likely remain unaltered. In the event that elevated levels of nitrite were concurrently available in drinking water contaminated by DIPA, there is a possibility for endogenous generation of *N*-nitrosobis(2-hydroxypropyl)amine.

Results of a long-term bioassay in rats suggest that relatively high levels of nitrite were required to initiate the production of sufficient quantities of this carcinogenic substance to produce tumors in tissues. No tumors developed, and no dose-response was observed when 0.15% soluble nitrite was given to rats that consumed DIPA in their diet. At 0.3% nitrite in drinking water, animals that received DIPA in the diet responded with significant increases in the number of tumors in several target tissues. Thus, there is a clear dose-response relationship between the consumption of DIPA and the amount of nitrite in drinking water.

The risk of developing genotoxic products endogenously is clearly related to the concentrations of key substances in the environment. The relationship between nitrite and DIPA in the environment will control the likelihood of the occurrence of a key event, or mutation in target tissues.

2.9.1.5 Reproduction and Developmental Studies

According to a Russian source, a study carried out in rats at a dose of 0.055 mg kg^{-1} bw day^{-1} revealed no effects on a number of markers of reproductive toxicity (BIBRA, 1991). This was based on an English language abstract of a paper in Russian. Since there is only one study, and it is unclear whether GLP criteria were used, we conclude there is insufficient data to assess whether DIPA exposure could produce adverse effects in reproductive endpoints.

2.9.1.6 Absorption, Tissue Distribution, Biotransformation, and Excretion

One study was available on the absorption, tissue distribution, and excretion of DIPA in mammals. A 19.5 mg^{-1} kg bw dose of ^{14}C-DIPA was dissolved in acetone and applied to the

skin of four female Fischer 344 rats (Dow, 1985b). After solvent evaporation, the DIPA remained in direct contact with the skin for 48 hours. At 48 hours, 25% of the DIPA had penetrated the skin and was absorbed. Approximately 12% of the applied dose was excreted unaltered by metabolism in the urine, 12.5% remained in tissues, and less that 1% was either eliminated in expired air or found in the feces. There was no evidence of DIPA accumulation in fatty tissues. Approximately 50% of the applied material was recovered from the skin, and about 23% was recovered from the skin at and around the site of application.

In the same study, a 19 mg kg^{-1} bw dose of aqueous ^{14}C-DIPA was administered intravenously to four female Fischer 344 rats. Greater than 70% of the radioactivity was cleared from the blood within the first six hours. Approximately 90% of the dose was recovered unchanged in urine within twelve hours. No metabolites of DIPA were characterized in urinary excretions (Dow, 1985b).

Metabolism studies of DIPA in animals indicate that it is poorly metabolized in mammals. Dow (1985b) concluded that DIPA, either ingested or absorbed through skin, would be eliminated rapidly and almost entirely in the urine.

2.9.2 Humans

2.9.2.1 Acute Toxicity Studies

Oral Studies

Acute oral studies on humans were not available in toxicity literature for DIPA.

Dermal and Ocular Studies

Responses to pure DIPA, or to a 1% aqueous solution in a patch test demonstrated variable skin irritation responses (BIBRA, 1991). A test of a sunscreen containing 1% DIPA on 24 human subjects that required 15 separate applications to skin over a 21 day period concluded the substance had minimal irritation qualities. However, in two other studies on human skin that required repeated application of a cream containing 1% DIPA, there was evidence of sensitization reactions. A number of dermal exposures were followed by a challenge to determine whether any subject responded with evidence of sensitization. It was concluded that the sunscreen product that contained DIPA was not a strong irritant, but that it may be capable of inducing contact sensitization (ACT, 1987).

Acute ocular studies on humans were not available in toxicity literature for DIPA.

2.9.2.2 Subchronic Toxicity Studies

Subchronic studies on humans were not available in toxicity literature for DIPA.

2.9.2.3 Chronic Toxicity and Oncogenicity Studies

Chronic toxicity and oncogenicity studies on humans were not available in toxicity literature for DIPA.

2.9.2.4 Genetic Toxicology Studies

Genetic toxicology studies on humans were not available in toxicity literature for DIPA.

2.9.2.5 Reproduction and Developmental Studies

Reproduction and developmental studies on humans were not available in toxicity literature for DIPA.

2.9.2.6 Absorption, Tissue Distribution, Biotransformation, and Excretion

Absorption, tissue distribution, biotransformation, and excretion studies on humans were not available in toxicity literature for DIPA.

3. DERIVATION OF ENVIRONMENTAL AND HUMAN HEALTH WATER QUALITY GUIDELINES

Environmental and human health water quality guidelines for DIPA are presented in Table 3.1.

3.1 Freshwater Aquatic Life

Freshwater aquatic life guidelines for DIPA were developed using the Protocol (*A Protocol for the Derivation of Water Quality Guidelines for the Protection of Aquatic Life*; CCME, 1999). The following sections summarize the requirements of the Protocol and discuss the available dataset in terms of these requirements. The toxicological dataset was summarized in Table 2.5, and discussed in Section 2.8.

The Protocol defines (1) the requirements for a toxicological study to be acceptable for guideline derivation (data quality requirement), (2) the minimum required dataset for Full and Interim guideline development (data quantity requirement), and (3) the process for deriving guidelines.

The following paragraphs provide a summary of the requirements of the Protocol, and assess the toxicological dataset.

3.1.1 Data Quality

The data quality requirement in the Protocol may be summarized as follows. For a toxicological study to be considered "Secondary Data", all relevant environmental variables (*e.g.*, temperature, pH, hardness, dissolved oxygen, etc.) should be measured and reported, and the survival of controls must be reported. In addition, for data to be considered "Primary Data", tests must employ currently acceptable practices, concentrations must be measured at the beginning and end of a test, and, in general, dynamic (*i.e.*, flow-through) tests are required. Data that do not conform to the requirements for Primary or Secondary Data are "Unacceptable Data".

The toxicological dataset is summarized in Table 2.5 and classified as Primary, Secondary, and Unacceptable. Only the work completed for this report conformed to all the requirements for Primary Data. The study by ERAC (1998) was classified as Secondary Data. All other studies were classified as Unacceptable Data. It should be noted that studies classified as "Unacceptable Data" may, in fact, represent acceptable (*i.e.*, Primary or Secondary) data, but insufficient information was available to confirm this. According to the Protocol only Primary or Secondary Data can be used in the guideline derivation process.

3.1.2 Data Quantity

The Protocol requirement for the quantity of Primary and/or Secondary Data for Interim freshwater aquatic life guidelines may be summarized as follows. At least two studies on freshwater fish species, and at least two studies on freshwater invertebrate species are required. The tests may be acute or chronic. One of the fish must be a cold water species, and two different classes of invertebrates must be represented, one of which includes a planktonic species resident in North America (*e.g.*, daphnid).

The Protocol requirements were met by the Primary and Secondary Data in Table 2.5. The acute tests on rainbow trout and fathead minnow fulfill the requirement for tests on two freshwater fish species, with the rainbow trout fulfilling the requirement for a cold water species. Acceptable test results are available for three species of invertebrate: *Daphnia magna* and *Ceriodaphnia dubia*, represent the Class Branchiopoda and *Hyalella azteca*, represent the Class Malacostraca.

Thus, all the Protocol requirements for data quantity were met.

3.1.3 Guideline Derivation

Note that the ERAC (1998) data at pH ">9" were not used in the guideline derivation process. See the end of this section for an explanation. The protocol defines procedures for deriving guidelines from both chronic and acute data. Guidelines were calculated from both acute and chronic data, and the lower value was adopted as the freshwater aquatic life guideline. A guideline is calculated from chronic data, by using the lowest LOEC from the most sensitive endpoint of the most sensitive lifestage of the most sensitive species, multiplied by a safety factor of 0.1 to give the freshwater aquatic life guideline. The lowest chronic LOEC for Primary or Secondary Data in this dataset is 16 mg L^{-1} for the 7 day reproduction endpoint for *Ceriodaphnia dubia*. This yields a guideline value of 1.6 mg L^{-1}.

A guideline can also be calculated from acute data, by using the lowest LC_{50} or EC_{50} value, and multiplying by an "application factor" of 0.05 for non-persistent variables. (DIPA would be considered a non-persistent variable because the majority of the data in Table 2.3 imply a biodegradation half-life of less than 8 weeks.) The lowest LC_{50} in the acute Primary or Secondary Data (excluding pH >9 data) in this dataset is 74 mg L^{-1} from the ERAC (1998) study on the 72 hour growth endpoint for *Selenastrum capricornutum*. Multiplying this value by an application factor of 0.05 gives a guideline of 3.7 mg L^{-1}. This value is higher than the guideline calculated from the chronic dataset, and thus the guideline of 3.1 mg L^{-1} from the chronic dataset is used (Table 3.1).

3.2 Marine Life

A marine life guideline for DIPA could not be developed using the Protocol ("*A Protocol for the Derivation of Water Quality Guidelines for the Protection of Aquatic Life*"; CCME, 1999) due to insufficient data quality and data quantity. The following sections summarize the requirements of the Protocol and discuss the available dataset in terms of these requirements. The toxicological dataset was summarized in Table 2.5, and discussed in Section 2.8.

The Protocol defines (1) the requirements for a toxicological study to be acceptable for guideline derivation (data quality requirement), (2) the minimum required dataset for Full and Interim guideline development (data quantity requirement), and (3) the process for deriving guidelines. The following paragraphs provide a summary of the requirements of the Protocol, and assess the toxicological dataset.

3.2.1 Data Quality

The data quality requirement in the Protocol may be summarized as follows. For a toxicological study to be considered "Secondary Data", all relevant environmental variables (*e.g.*, temperature,

pH, hardness, dissolved oxygen, etc.) should be measured and reported, and the survival of controls must be reported. In addition, for data to be considered "Primary Data", tests must employ currently acceptable practices, concentrations must be measured at the beginning and end of a test, and, in general, dynamic (*i.e.*, flow-through) tests are required. Data that do not conform to the requirements for Primary or Secondary Data are "Unacceptable Data".

The toxicological dataset is summarized in Table 2.5 and all studies were classified as Unacceptable. It should be noted that studies classified as "Unacceptable Data" may, in fact, represent acceptable (*i.e.*, Primary or Secondary) data, but insufficient information was available to confirm this. According to the Protocol only Primary or Secondary Data can be used in the guideline derivation process. Therefore, a marine life water quality guideline for DIPA could not be developed.

3.2.2 Data Quantity

Since Primary or Secondary studies on marine life were not available in the toxicological literature, the marine life guideline could not be developed. The Protocol requirement for the quantity of Primary and/or Secondary Data for Interim marine life guidelines may be summarized as follows. At least two studies on marine fish species, and at least two studies on marine invertebrate species are required. The tests may be acute or chronic. One of the fish must be a temperate species, and two different classes of invertebrates must be represented.

The Protocol data quantity requirements were not met by the data in Table 2.5.

3.2.3 Guideline Derivation

A marine life guideline for DIPA could not be developed using the Protocol due to insufficient data quality and data quantity.

3.3 Irrigation

Irrigation water quality guidelines for DIPA were developed using the Protocol ("*Protocols for Deriving Water Quality Guidelines for the Protection of Agricultural Water Uses*"; CCME, 1999). The toxicological data set was sufficient to derive Interim guidelines (Table 2.4). Data in Table 2.4 are classified as primary toxicological data by the Protocol. As laid out in the Protocol, irrigation guidelines were calculated for (1) tame hay, cereal, and pasture crops (*e.g.*, alfalfa and timothy) and (2) other crops (*e.g.*, lettuce and carrot).

As can be seen in Table 2.4, the sensitivity of plants to DIPA varies strongly depending on soil type. For most plant species and endpoints, plants were most sensitive to DIPA in sand or till, and least sensitive in loam. Accordingly, guidelines were calculated for "poor soil" (*i.e.*, sand or till), and loam. The reason for this approach was to provide both an overall irrigation guideline, which was protective of crop growth on any soil type, and guidance on tolerable levels of DIPA when crops are being grown on typical, improved, agricultural soils.

Four guidelines are presented in Table 3.1, including the two soil types (poor soil and loam) and two crop types (tame hay, cereal, and pasture crops and other crops) noted above. The overall irrigation guideline is the lowest of these four guidelines. The detailed guideline derivation process is described below.

The first step in the guideline derivation process was the calculation of the acceptable soil concentration (ASC), which is an estimate of the soil concentration that would not result in adverse effects on crops over the course of one growing season:

$$ASC\ (mg\ kg^{-1}) = \left(\frac{\sqrt{LOEC \times NOEC}}{UF} \right)$$

Where: LOEC = lowest-observed-effect-concentration (mg kg^{-1} soil);
NOEC = no-observed-effect-concentration (mg kg^{-1} soil); and,
UF = uncertainty factor of 10.

The calculated ASCs were as follows:

- 56 mg kg^{-1} for cereals, tame hays, and pasture crops grown in loam, based on the root length endpoint for alfalfa;
- 48 mg kg^{-1} for cereals, tame hays, and pasture crops grown in poor soil, based on the biomass endpoint for timothy in sand;
- 224 mg kg^{-1} for other crops grown in loam, based on the root length endpoint for lettuce; and,
- 24 mg kg^{-1} for other crops grown in poor soil, based on the root length endpoint for lettuce and carrot in sand.

The next step in the guideline derivation process is to calculate species maximum acceptable toxicant concentration (SMATC), which is the maximum amount of contaminant allowed in a 1 ha (100 m x 100 m) plot. The SMATC is calculated as:

$$SMATC\ (mg\ L^{-1}) = \left(\frac{ASC \times \rho \times L \times W \times D}{IR} \right)$$

Where: ASC = acceptable soil concentration (mg kg^{-1}; calculated above);
ρ = soil bulk density (1,300 kg m^{-3});
L = length (100 m);
W = width (100 m);
D = depth (1.5 m for tame hays, cereals, and pasture crops, and 0.15 m for other crops); and,
IR = irrigation rate per year (1.2×10^7 L ha^{-1}).

The SMATC for cereals, tame hays, and pasture crops was 91 mg L^{-1} (loam), and 78 mg L^{-1} (poor soil). For other crops the SMATC was 36 mg L^{-1} (loam), and 3.9 mg L^{-1} (poor soil). These values are proposed as Interim Irrigation water quality guidelines for DIPA (Table 3.1).

3.4 Livestock Watering

Livestock watering guidelines for DIPA were developed using the Protocol ("*Protocols for Deriving Water Quality Guidelines for the Protection of Agricultural Water Uses*", CCME, 1999). The following sections summarize the requirements of the Protocol and discuss the available dataset in terms of these requirements. The toxicological dataset is summarized in Table 2.6, and discussed in Section 2.9.

The Protocol defines (1) the requirements for a toxicological study to be acceptable for guideline derivation (data quality requirement), (2) the minimum required dataset for Full and Interim guideline development (data quantity requirement), and (3) the process for deriving guidelines. The following paragraphs provide a summary of the requirements of the Protocol, and assess the toxicological dataset.

3.4.1 Data Quality

The data quality requirement in the Protocol may be summarized as follows. For a toxicological study to be considered "Secondary Data", the dose, duration of exposure, and effects should be reported, the response and survival of controls must be reported. Secondary Data may be for any route of exposure (*e.g.*, oral, inhalation, dermal). Secondary Data does not have to conform to accepted laboratory practices as long as all necessary information is reported. For data to be considered "Primary Data", tests must employ currently acceptable laboratory practices, report dose in standard units (*i.e.*, mg kg^{-1} bw day^{-1} for chronic tests and mg kg^{-1} bw for acute tests), report the response and survival of controls, report the scientifically valid statistics used. In addition, it is preferred that Primary Data have (1) doses measured analytically, (2) be through a simulated drinking water exposure (*e.g.*, *ad libitum*, gavage, oesophageal cannula, or rumen

fistula of food and water), (3) be full life cycle studies, and (4) examine sensitive endpoints (*e.g.*, development, growth, fecundity) and production parameters (*e.g.*, milk yield, litter size, feed conversion). Data that do not conform to the requirements for Primary or Secondary Data are "Unacceptable Data".

The toxicological dataset is summarized in Table 2.6 and classified as Primary, Secondary, or Unacceptable. Primary and Secondary Data were available for the rat, mouse, guinea pig, and rabbit. Eight acute, two subchronic, and two chronic Primary Data studies were available. Acute effects ranged from 2,120 to 6,720 mg kg^{-1} bw. Subchronic and chronic NOAELs for DIPA alone ranged from 0.22 to 600 mg kg^{-1} bw day^{-1}.

3.4.2 Data Quantity

The Protocol requirement for the quantity of Primary and/or Secondary Data for an Interim livestock watering guideline was two studies on two or more mammalian species, one of which should be a livestock species, and one study on one or more avian livestock species. The tests can be acute or chronic. The species must be raised in Canada.

According to the Protocol data quantity requirements, there is insufficient data to derive an Interim guideline. However, the data quality was such that a "Preliminary" guideline was developed. The Preliminary guideline was developed following the Protocol by using the non-livestock mammalian toxicity data.

3.4.3 Guideline Derivation

The TDI was based on acute toxicological data from laboratory animals (Table 2.6). The mean and standard deviation for five acute studies on three species was 4,260 ± 1,920 mg kg^{-1} bw day^{-1}. The dermal study reported by Union Carbide (1973) was not included due the large LD_{50} resulting from lowered bioavailability.

The first step in the guideline derivation process was the calculation of the TDI, which was based on an extrapolation of acute to chronic data (CCME, 1999):

$$TDI\ (mg\ kg^{-1}\ bw\ day^{-1}) = \left(\frac{LD_{50}}{70 \times UF}\right)$$

Where: LD_{50} = lethal dose to 50% of the population (4,260 mg kg^{-1} bw day^{-1}; Table 2.6);
70 = extrapolation factor from acute to chronic data (CCME, 1999); and,
UF = uncertainty factor (10; CCME, 1999).

Based on the acute to chronic extrapolation, the TDI for DIPA applicable to livestock is 6.1 mg kg^{-1} bw day^{-1}. The chronic NOAEL reported by Yamamoto *et al.* (1989) was 391 mg kg^{-1} bw day^{-1} which, after applying the 10-fold uncertainty factor recommended by CCME (1999), yields a TDI of 39 mg kg^{-1} bw day^{-1}. The TDI calculated using the acute to chronic extrapolation method was an order of magnitude more protective and was used to develop the DIPA livestock watering guideline.

The next step in the guideline derivation process was to calculate the reference concentration (RC), which represents the livestock watering guideline. The reference concentration is calculated using the body weight and water ingestion rate of particular species. Dairy cattle and beef cattle were selected to represent livestock; deer were also considered to help assess possible risks to other species. The equation used was:

$$RC\ (mg\ L^{-1}) = \left(\frac{TDI \times BW}{WIR}\right)$$

Where: TDI = tolerable daily intake for DIPA (6.1 mg kg^{-1} day^{-1}; calculated above);
BW = body weight (862 kg for dairy cattle (CCME, 1999), 730 kg for beef cattle (CCME, 1999), and 68 kg for deer (Smith, 1993); and,
WIR = daily water intake rate (137 L day^{-1} for dairy cattle, CCME (1999), data for lactating cows at 21° C), 80 L day^{-1} for beef cattle (CCME, 1999), and 4.4 L day^{-1} for deer (Smith, 1993).

The RCs for dairy cattle, beef cattle, and deer were 38, 56, and 94 mg L^{-1} DIPA, respectively. These values are recommend for the livestock watering guidelines (Table 3.1).

3.5 Source Water for Drinking

The generic scenario assumed to develop source water for drinking guidelines was the "Agricultural Land Use" scenario defined by the Protocol. This scenario assumes a multi-functional farm with a family with children resident on the property. The farm grows produce, raises livestock, has a dairy herd and a large proportion of the produce (50%), meat (50%), and milk (100%) consumed by the family is produced on the farm. It is assumed here that groundwater is used for drinking water. For DIPA, the most sensitive human receptor would be a child.

Humans could be exposed to DIPA in groundwater by (1) ingestion of drinking water and water used for cooking and (2) dermal contact during bathing and washing. While individuals could be

exposed to DIPA in surface water through swimming and/or fishing, this exposure pathway will be minimal relative to those noted above. A dermal contact check is provided to evaluate the relative importance of this exposure pathway.

3.5.1 Tolerable Daily Intake (TDI)

The Protocol defines the Tolerable Daily Intake (TDI) as the intake to which it is believed a receptor can be exposed over a lifetime without deleterious effects. The TDI represents the combination of (1) real values for toxicological endpoints when no evidence of adverse effects can be detected in experimental animals or humans and (2) safety factors that account for anticipated differences between responses in the species tested and humans, sensitive individuals in the human population, and other factors that contribute to the uncertainty of the toxicological data.

The TDI is defined by the Protocol as:

$$TDI = \left(\frac{LOAEL \text{ or } NOAEL}{Safety\ Factor} \right)$$

The conversion of toxicological data from the laboratory into values or rates of exposure acceptable for human health assessment requires the introduction of safety factors. These factors account for uncertainties that arise from differences between laboratory animals and humans, sensitivity of populations, and experience. The introduction of safety factors is a concept that has had wide acceptance in the scientific and regulatory communities around the world.

The Joint European Committee on Food Additives (JECFA) proposed principles for determining a margin of safety, and has developed a methodology to establish an acceptable value for a factor that would directly link animal toxicological data to human health and safety (FAO/WHO, 1958). The margin of safety allows for any interspecies differences in susceptibility, the numerical differences between the test animals and the exposed human population, the greater variety of complicating disease processes in the human population, the difficulty of estimating the human intake, and the possibility of synergistic action. JECFA stated that the 100-fold margin of safety applied to the maximum ineffective dosage (expressed in mg kg^{-1} body weight day^{-1}) was believed to be an adequate factor (FAO/WHO, 1958). The value of 100 has been regarded as comprising two factors of ten to allow for interspecies and intraspecies variation (WHO, 1994).

The validity and size of safety/uncertainty factors, and their application across many substances including pesticides has undergone periodic reevaluation (Renwick and Lazarus, 1998). By and

large, the allocation of appropriate safety factors is considered on a case-by-case basis, relying on analysis of the total weight of evidence including a consideration of data gaps (WHO, 1990). WHO Scientific Groups have confirmed a 100-fold safety factor as an adequate and useful guide, particularly when there are few toxicological data gaps (WHO, 1967; 1994).

The National Research Council report on Pesticides in the Diets of Infants and Children (NRC, 1993) indicated that the current 10-fold intraspecies factor is adequately protective of socioeconomic, nutritional, and health status factors that influence the vulnerability of children to environmental toxicants.

3.5.1.1 Human Tolerable Daily Intake (TDI)

The availability of toxicological data for DIPA would suggest that, for humans, application of a 10-fold safety factor for interspecies differences, and a 10-fold factor for variability in the sensitivity of the human population is warranted. Because of the uncertainty associated with the variable level of nitrite in the diet, and the possible endogenous production of genotoxic substances, we recommend an additional five-fold safety factor to protect children and developing infants (newborns and fetuses). Thus, a 500-fold safety factor was applied to the Yamamoto *et al.* (1989) chronic NOAEL of 391 mg kg^{-1} bw day^{-1} to derive a tolerable daily intake of 0.78 mg kg^{-1} bw day^{-1}.

3.5.1.2 Bioavailability

Data were not available to derive an oral bioavailability factor for DIPA. As a result, a bioavailability of 100% has been assumed for oral exposures. Dow (1985b) has established a dermal bioavailability factor of 25%. This factor was used in guideline derivation.

3.5.2 Guideline Development

The absorbed dose from ingestion of DIPA in source water for drinking was calculated for humans and livestock using (US EPA, 1989; CCME, 1996):

$$Dose\ (mg\ kg^{-1}\ bw\ day^{-1}) = \left(\frac{C_W \cdot IR_W \cdot BIO_O \cdot EF}{BW \cdot AT} \right)$$

Where: C_W = concentration of DIPA in water (mg L^{-1});
IR_W = drinking water ingestion rate (0.6 L day^{-1} (child, 0.5 to 5 years) and 1.5 L day^{-1} (adult); CCME, 2000);
BIO_O = oral bioavailability (1; assumed);

EF = exposure frequency (365 days; assumed);
BW = receptor body weight (16 kg (child, 0.5 to 5 years) and 70.7 kg (adult); CCME, 2000); and,
AT = averaging time (365 days; assumed).

The above formula was re-arranged to yield the source water for drinking guidelines (US EPA, 1989; CCME, 1996):

$$Drinking\ Water\ Guideline\ (mg \cdot L^{-1}) = \left(\frac{BW \cdot TDI}{IR_W \cdot BIO_O} \right)$$

Where:
BW = receptor body weight (16 kg (child, 0.5 to 5 years) and 70.7 kg (adult); CCME, 2000);
TDI = tolerable daily intake (0.78 mg kg^{-1} bw day^{-1});
IR_W = drinking water ingestion rate (0.6 L day^{-1} (child, 0.5 to 5 years) and 1.5 L day^{-1} (adult); CCME, 2000); and,
BIO_O = oral bioavailability (1; assumed).

For a child and an adult, the proposed Interim source water for drinking guidelines are 21 mg L^{-1} and 37 mg L^{-1}, respectively. The guideline protective of a child is reported in Table 3.1.

3.5.3 Dermal Contact Check

To determine if dermal contact was a significant exposure route relative to oral ingestion, dermal exposure modelling was conducted following US EPA (1992, 1997). Dermal exposure modelling is concerned with absorption and transport of chemicals through the outer skin layer (stratum corneum) and into the viable epidermis. The stratum corneum is the primary barrier to dermal absorption. This layer consists of a protein (keratin) and lipid matrix that channels chemicals through transcellular (aqueous) and intercellular (lipid) pathways.

The absorbed dose from dermal contact with DIPA for a child during bathing was calculated using (US EPA, 1992):

$$Dose\ (mg\ kg^{-1}\ bw\ day^{-1}) = \frac{C_W \cdot SA \cdot ET \cdot PC \cdot EF}{BW \cdot AT \cdot 1000}$$

Where:
C_W = concentration of DIPA in water (mg L^{-1});
SA = skin surface area exposed during bathing (7,640 cm^2 95th percentile for whole body for 3 to 4 year old child; US EPA, 1992);

ET = length of time the skin is in contact with water (0.5 hours day^{-1}; assumed);
PC = chemical specific dermal permeability constant (0.0003 cm hour-1; calculated);
EF = exposure frequency (365 days; assumed);
BW = receptor body weight (16 kg; CCME, 2000); and,
AT = averaging time (365 days; assumed).
The value of 1000 was used to convert from cm^3 to L.

The chemical-specific dermal permeability constant (PC) for DIPA was estimated using (US EPA, 1992):

$$Log\ PC\ (cm\ hour^{-1}) = -2.72 + 0.71 \log K_{OW} - 0.0061\ MW$$

Where: $\log K_{ow}$ = *n*-octanol-water partition coefficient (-0.072, unitless); and,
MW = molecular weight (133.19 g mol^{-1}).

Using the chemical/physical properties noted above (see also Table 2.2), the estimated dermal permeability constant for DIPA was 0.0003 cm $hour^{-1}$.

Assuming a DIPA concentration in water of 1 mg L^{-1}, and assuming a 0.5-hour bath each day, the calculated absorbed dermal dose for a child was 7 x 10^{-5} mg kg^{-1} bw day^{-1}. The calculated absorbed dose for a child drinking water was 0.038 mg kg^{-1} bw day^{-1}, assuming 1 mg L^{-1} DIPA concentration in the source water for drinking supply. Therefore, the dermal pathway accounts for approximately 0.2% of the oral dose and can be safely ignored.

3.6 Data Gaps

3.6.1 Freshwater Aquatic Life

The dataset for freshwater aquatic life was sufficient to derive Interim guidelines. For a Full freshwater aquatic life guideline to be developed, the following additional studies would be required:

- two chronic studies on freshwater fish species resident in North America;
- two chronic studies on two invertebrate species from different classes, one of which was a planktonic species resident in North America (*e.g.*, a daphnid); and,
- one study on a freshwater vascular plant or algal species resident in North America.

All the studies for a Full guideline must be of Primary data quality.

3.6.2 Marine Aquatic Life

The dataset for marine aquatic life guideline was not sufficient to derive Interim guidelines. The following additional toxicity tests would be required:

- two acute or chronic studies on different marine fish species, including one temperate species; and,
- two acute or chronic studies on temperate marine invertebrate species from two different classes.

For a Full marine guideline to be developed, the following additional studies would be required:

- three studies on three species of temperate marine fish of which at least two are chronic;
- two chronic studies on two temperate marine invertebrate species from different classes; and,
- one study on a temperate marine vascular plant or algal species.

All the studies for a Full guideline must be of Primary data quality.

3.6.3 Irrigation

Sufficient data were available to meet the requirements for the Interim irrigation guideline.

3.6.4 Livestock Watering

To comply with the requirements of the Protocol for an Interim livestock watering guideline, the following additional studies would be required:

- two acute or chronic studies on mammalian species raised in Canada, of which one is a livestock species; and,
- one acute or chronic study on an avian livestock species.

In spite of this deficiency, a Preliminary livestock watering guideline was derived, based on laboratory animal studies.

3.6.5 Source Water for Drinking

Sufficient data were available to calculate the Interim source water for drinking guideline for DIPA.

3.7 Summary of Water Quality Guidelines

Water quality guidelines were calculated for four water uses: freshwater aquatic life, irrigation, livestock watering, and source water for drinking. The recommended guidelines are summarized in Table 3.1.

3.7.1 Freshwater Aquatic Life

The Interim guideline for freshwater aquatic life was calculated to be 1.6 mg L^{-1}.

3.7.2 Marine Life

A guideline for marine life could not be developed due to insufficient data quality and data quantity.

3.7.3 Irrigation

Four guidelines were calculated for irrigation. Based on the Protocol, Interim guidelines were calculated for 1) cereals, tame hays, and pasture crops, and 2) other crops. For each of these two groups of plants, guidelines were calculated for two soil types: loam and poor soil. The guideline for cereals, tame hays, and pasture crops was 91 mg L^{-1} (loam) and 78 mg L^{-1} (poor soil). For other crops it was 36 mg L^{-1} (loam), and 3.9 mg L^{-1} (poor soil).

3.7.4 Livestock Watering

Preliminary guidelines for livestock watering were calculated for dairy cattle and beef cattle, to represent likely agricultural animals. In addition, a Preliminary guideline was calculated for deer, to assist in evaluating possible risks to other species. The most sensitive species was the dairy cow, for which a guideline of 38 mg L^{-1} was calculated. The reason for the difference in sensitivity between life stages or species is related to how water consumption relates to body weight. In a situation where water was being used for the consumption of a single livestock species other than cattle, typical water ingestion rates and body weight could be used to calculate a species-specific guideline. It should be noted that this guideline was based on studies on laboratory animals using appropriate safety factors, and no toxicological information was available for either a mammalian or avian livestock species. Should sufficient data become available in the future, this guideline could be refined.

3.7.5 Source Water for Drinking

Interim source water for drinking guidelines were calculated for children (21 mg L^{-1}) and adults (37 mg L^{-1}). If further mammalian toxicological studies become available in the future, this guideline could be refined.

4. CLOSURE

The information presented in this report was produced exclusively for the purposes stated in the Scope of Work. Komex International Ltd. provided this groundwater derivation document for British Columbia Ministry of Water, Land and Air Protection, solely for the purpose noted above, and does not accept any responsibility for the use of this report for any purpose other than intended or to any third party.

Komex International Ltd. has exercised reasonable skill, care, and diligence to assess the information acquired during the preparation of this report. The methodology used deriving the guidelines in this report is based on current regulatory protocols and current understanding of biological systems, mechanisms of exposure, and toxicological properties of chemicals.

Questions concerning the derivation or use of the guidelines in this report should be directed to Dr. James H. Sevigny, Mr. Miles Tindal, or Ms. Adele Houston.

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TABLES

Table 2.1. Common Synonyms and Trade Names for Diisopropanolamine

Synonyms	
Bis(2-hydroxypropyl)amine	1,1'-Iminodi-2-propanol
Bis(2-propanol)amine	1,1'-Iminodipropan-2-ol
DIPA	2-Propanol, 1,1'iminobis-
Dipropyl-2,2-dihydroxy-amine	2-Propanol, 1,1'-iminodi-
1,1'-Iminobis(2-propanol)	

Source: NIST Chemistry WebBook (2000)

Table 2.2. Physical and Chemical Properties for Diisopropanolamine

Property	*Value*	*Units*	*Reference*
CAS registry number	110-97-4	-	
Molecular formula	$C_6H_{15}NO_2$	-	Lide (1996)
Molecular weight	133.19	g/mole	Lide (1996)
Melting point	44	° C	Kirk-Othmer (1999)
Boiling point	249	° C	Kirk-Othmer (1999)
Specific gravity			
20° C (DIPA) /4° C (Water)	1.004	-	Aldrich (1990)
40° C (DIPA) /4° C (Water)	0.992	-	Dow (1999)
Flashpoint	126 (closed up)	° C	Lenga, 1985
Density at 25° C	0.989	g/cm^3	Lide (1996)
Vapour density (air=1)	4.6	g/L	Verschueren (1996)
Vapour pressure			
42° C	0.02	mm Hg	Verschueren (1996)
50° C	0.035	mm Hg	Dow (1999)
100° C	3	hPA	Verschueren (1996)
n-Octanol-water partition coefficient (K_{ow})	-0.072	log	Dow (1995)
Organic carbon partition coefficient (K_{oc})	21.77	log	Dow (1995)
Henry's law constant	1.72×10^{-7}	atm x m^3/mol	Dow (1995)
Solubility in water			
25° C	1,200	g/100g	Kirk-Othmer (1999)
25° C	870	g/L	Verschueren (1996)
Water soil partition coefficient (K_d)			
montmorillonite	16-42	L/kg	Luther *et al.* (1998)
kaolinite	3.5	L/kg	Luther *et al.* (1998)
humus-rich soil	2.0	L/kg	Luther *et al.* (1998)
low carbon content surface soils	0.73 - 4.0	L/kg	Luther *et al.* (1998)
till	3.2	L/kg	Luther *et al.* (1998)
sandstone, shale/sandstone	0.54 - 1.1	L/kg	Luther *et al.* (1998)
pKa	8.88	-log K	Kim *et al.* (1987)
Viscosity			
30° C	870	centipoise	Sorensen *et al.* (1996)
54° C	86	centipoise	Kirk-Othmer (1999)

Table 2.3. Biodegradation Studies for Diisopropanolamine

Study	*Concentration* [1] *(mg L^{-1})*	*Microcosm Material*	*Conditions*	*Nutrients*	*Temperature (°C)*	*Lag Time (days)*	*Biodegradation Rate (mg L^{-1} day^{-1})*
Salanitro and Langston (1988)	75	Sandy loam	aerobic	N, P	10	7 to 14	10 [2]
Chong (1994)	260	Activated sludge	aerobic	N, P	25	6	70
Gieg *et al.* (1998)	200	Sandstone	aerobic	N, P	8	na	6.3 [2]
Gieg *et al.* (1998)	200	Sandstone	aerobic	N, P	28	na	2.7 [2]
Gieg *et al.* (1998)	200	Till	aerobic	N, P	8	na	1.5 [2]
Gieg *et al.* (1998)	200	Sand	aerobic	N, P	8	na	1.7 [2]
Gieg *et al.* (1998)	200	Sand	aerobic	N, P	28	na	0.6 [2]
Greene *et al.* (1999) [3]	490	Till	aerobic	none	8	220	0
Greene *et al.* (1999) [3]	490	Till	aerobic	P	8	na	5.3
Greene *et al.* (1999) [3]	680	Till	aerobic	none	8	220	0
Greene *et al.* (1999) [3]	680	Till	aerobic	P	8	15	3.6
Greene *et al.* (1999) [3]	0.0024	Wetland sediment	aerobic	none	8	<1	1.4
Greene *et al.* (1999) [3]	0.013	Wetland sediment	aerobic	none	8	14	0.5

(1) = minimum concentration reported. (2) = reported at half-life in days. (3)= data reported for 2.5 L microcosms. na = not available.

Nutrients: N = nitrogen; P = phosphorous

Table 2.4. Toxicity of Diisopropanolamine to Terrestrial Plants

Species	Scientific Name	Endpoint	Soil Type	NOEC ($mg\ kg^{-1}$)	LOEC ($mg\ kg^{-1}$)	EC_{25} ($mg\ kg^{-1}$)	EC_{50} ($mg\ kg^{-1}$)	Reference
Lettuce	*Lactuca sativa*	root elongation	Till	140	na	na	600	Komex (1999)
Lettuce	*Lactuca sativa*	germination	Till	6,300	na	na	9,400	Komex (1999)
Lettuce	*Lactuca sativa*	emergence	Artificial	1,750	3,490	1,310	3,840	CAPP (2001)
Lettuce	*Lactuca sativa*	emergence	Loam	10,400	20,800	15,400	20,400	CAPP (2001)
Lettuce	*Lactuca sativa*	emergence	Sand	1,700	3,390	1,700	2,260	CAPP (2001)
Lettuce	*Lactuca sativa*	emergence	Till	3,480	6,970	4,830	6,210	CAPP (2001)
Lettuce	*Lactuca sativa*	biomass	Artificial	3,490	6,980	4,530	>6,980	CAPP (2001)
Lettuce	*Lactuca sativa*	biomass	Loam	10,400	20,800	15,800	>20,800	CAPP (2001)
Lettuce	*Lactuca sativa*	biomass	Sand	1,700	>1,700	>1,700	>1,700	CAPP (2001)
Lettuce	*Lactuca sativa*	biomass	Till	3,480	6,970	810	5,480	CAPP (2001)
Lettuce	*Lactuca sativa*	root length	Artificial	873	1,750	1,220	3,750	CAPP (2001)
Lettuce	*Lactuca sativa*	root length	Loam	2,600	5,200	5,660	14,000	CAPP (2001)
Lettuce	*Lactuca sativa*	root length	Sand	212	424	635	1,391	CAPP (2001)
Lettuce	*Lactuca sativa*	root length	Till	1,740	3,480	2,100	2,930	CAPP (2001)
Lettuce	*Lactuca sativa*	shoot length	Artificial	3,490	6,980	5,820	>6,980	CAPP (2001)
Lettuce	*Lactuca sativa*	shoot length	Loam	20,800	>20,800	>20,800	>20,800	CAPP (2001)
Lettuce	*Lactuca sativa*	shoot length	Sand	1,700	>1,700	>1,700	>1,700	CAPP (2001)
Lettuce	*Lactuca sativa*	shoot length	Till	3,480	6,970	5,230	>6,970	CAPP (2001)
Minimum Toxicity Values for Lettuce				***140***	***424***	***635***	***600***	

na = not available

Table 2.4. Toxicity of Diisopropanolamine to Terrestrial Plants (Cont'd)

Species	Scientific Name	Endpoint	Soil Type	NOEC (mg kg^{-1})	LOEC (mg kg^{-1})	EC_{25} (mg kg^{-1})	EC_{50} (mg kg^{-1})	Reference
Carrot	*Daucus carota*	emergence	Artificial	3,490	6,980	4,280	6,980	CAPP (2001)
Carrot	*Daucus carota*	emergence	Loam	5,460	10,900	8,700	24,600	CAPP (2001)
Carrot	*Daucus carota*	emergence	Sand	1,700	3,390	2,280	2,870	CAPP (2001)
Carrot	*Daucus carota*	emergence	Till	3,480	6,970	4,290	5,180	CAPP (2001)
Carrot	*Daucus carota*	biomass	Artificial	6,980	>6,980	>6,980	>6,980	CAPP (2001)
Carrot	*Daucus carota*	biomass	Loam	21,900	>21,900	>21,900	>21,900	CAPP (2001)
Carrot	*Daucus carota*	biomass	Sand	3,390	>3,390	>3,390	>3,390	CAPP (2001)
Carrot	*Daucus carota*	biomass	Till	3,480	>3,480	>3,480	>3,480	CAPP (2001)
Carrot	*Daucus carota*	root length	Artificial	873	1,750	1,880	3,670	CAPP (2001)
Carrot	*Daucus carota*	root length	Loam	5,460	10,900	8,510	12,000	CAPP (2001)
Carrot	*Daucus carota*	root length	Sand	212	424	355	1,810	CAPP (2001)
Carrot	*Daucus carota*	root length	Till	1,710	3,480	2,050	>3,480	CAPP (2001)
Carrot	*Daucus carota*	shoot length	Artificial	3,490	6,980	4,890	>9,890	CAPP (2001)
Carrot	*Daucus carota*	shoot length	Loam	10,900	21,900	17,000	>21,900	CAPP (2001)
Carrot	*Daucus carota*	shoot length	Sand	1,700	3,390	2,140	3,360	CAPP (2001)
Carrot	*Daucus carota*	shoot length	Till	3,480	>3,480	>3,480	>3,480	CAPP (2001)
Minimum Toxicity Values for Carrot				***212***	***424***	***355***	***1,810***	

na = not available

Table 2.4. Toxicity of Diisopropanolamine to Terrestrial Plants (Cont'd)

Species	Scientific Name	Endpoint	Soil Type	NOEC ($mg\ kg^{-1}$)	LOEC ($mg\ kg^{-1}$)	EC_{25} ($mg\ kg^{-1}$)	EC_{50} ($mg\ kg^{-1}$)	Reference
Alfalfa	*Medicago sativa*	emergence	Artificial	6,980	14,000	7,310	9,540	CAPP (2001)
Alfalfa	*Medicago sativa*	emergence	Loam	10,400	20,800	14,300	20,400	CAPP (2001)
Alfalfa	*Medicago sativa*	emergence	Sand	1,700	3,390	2,000	2,460	CAPP (2001)
Alfalfa	*Medicago sativa*	emergence	Till	3,480	6,970	3,620	4,740	CAPP (2001)
Alfalfa	*Medicago sativa*	biomass	Artificial	6,980	>6,980	>6,980	>6,980	CAPP (2001)
Alfalfa	*Medicago sativa*	biomass	Loam	10,400	20,800	14,200	>20,800	CAPP (2001)
Alfalfa	*Medicago sativa*	biomass	Sand	1,700	>1,700	>1,700	>1,700	CAPP (2001)
Alfalfa	*Medicago sativa*	biomass	Till	3,480	6,970	810	5,480	CAPP (2001)
Alfalfa	*Medicago sativa*	root length	Artificial	873	1,750	1,590	2,780	CAPP (2001)
Alfalfa	*Medicago sativa*	root length	Loam	650	1,300	1,580	9,240	CAPP (2001)
Alfalfa	*Medicago sativa*	root length	Sand	424	848	718	>1,700	CAPP (2001)
Alfalfa	*Medicago sativa*	root length	Till	871	1,740	1,410	2,780	CAPP (2001)
Alfalfa	*Medicago sativa*	shoot length	Artificial	1,750	3,490	4,760	>6,980	CAPP (2001)
Alfalfa	*Medicago sativa*	shoot length	Loam	20,800	>20,800	17,800	>20,800	CAPP (2001)
Alfalfa	*Medicago sativa*	shoot length	Sand	1,700	>1,700	>1,700	>1,700	CAPP (2001)
Alfalfa	*Medicago sativa*	shoot length	Till	3,480	>3,480	>3,480	>3,480	CAPP (2001)
Minimum Toxicity Values for Alfalfa				***424***	***848***	***718***	***>1,700***	

na = not available

Table 2.4. Toxicity of Diisopropanolamine to Terrestrial Plants (Cont'd)

Species	Scientific Name	Endpoint	Soil Type	NOEC ($mg\ kg^{-1}$)	LOEC ($mg\ kg^{-1}$)	EC_{25} ($mg\ kg^{-1}$)	EC_{50} ($mg\ kg^{-1}$)	Reference
Timothy	*Phleum pratense*	emergence	Artificial	3,490	6,980	5,850	8,430	CAPP (2001)
Timothy	*Phleum pratense*	emergence	Loam	21,900	43,700	25,600	32,200	CAPP (2001)
Timothy	*Phleum pratense*	emergence	Sand	1,700	3,390	2,340	2,980	CAPP (2001)
Timothy	*Phleum pratense*	emergence	Till	3,480	6,970	6,530	9,070	CAPP (2001)
Timothy	*Phleum pratense*	biomass	Artificial	1,750	3,490	1,950	3,230	CAPP (2001)
Timothy	*Phleum pratense*	biomass	Loam	10,900	21,900	9,680	>43,700	CAPP (2001)
Timothy	*Phleum pratense*	biomass	Sand	424	847	606	1,680	CAPP (2001)
Timothy	*Phleum pratense*	biomass	Till	6,970	>6,970	>6,970	>6,970	CAPP (2001)
Timothy	*Phleum pratense*	root length	Artificial	1,750	3,490	4,080	5,290	CAPP (2001)
Timothy	*Phleum pratense*	root length	Loam	10,900	21,900	1,820	20,900	CAPP (2001)
Timothy	*Phleum pratense*	root length	Sand	424	874	1,590	2,260	CAPP (2001)
Timothy	*Phleum pratense*	root length	Till	na	na	na	na	CAPP (2001)
Timothy	*Phleum pratense*	shoot length	Artificial	1,750	3,490	3,830	5,700	CAPP (2001)
Timothy	*Phleum pratense*	shoot length	Loam	10,900	21,900	15,200	19,600	CAPP (2001)
Timothy	*Phleum pratense*	shoot length	Sand	847	1,700	1,870	2,790	CAPP (2001)
Timothy	*Phleum pratense*	shoot length	Till	3,480	6,970	4,490	6,090	CAPP (2001)
Minimum Toxicity Values for Timothy				***424***	***874***	***606***	***1,680***	

na = not available

Table 2.5. Toxicity of Diisopropanolamine to Aquatic Species

Type of Study	Type of Biota	Common Name	Species	Duration	Endpoint	NOEC (mg L^{-1})	LOEC (mg L^{-1})	LC_{50}/EC_{50} (mg L^{-1})	Temperature	pH	DO (mg L^{-1})	Hardness (mg L^{-1})	Controls Acceptable?	Chemical Analysis?	Experimental Design	Protocol	Reference
								Primary Freshwater Data									
acute	vertebrate	rainbow trout	*Oncorhynchus mykiss*	96 hours	survival			7,698	15±1	7.5	na	255	S	Y	S	ECP	CAPP, 2001
acute	vertebrate	rainbow trout	*Oncorhynchus mykiss*	96 hours	survival			4,940	15±1	8.5	na	255	S	Y	S	ECP	CAPP, 2001
acute	invertebrate	sideswimmer	*Hyalella azteca*	96 hours	survival			1,128	23±1	7.5	na	255	S	Y	S	(ECP)	CAPP, 2001
acute	invertebrate	sideswimmer	*Hyalella azteca*	96 hours	survival			848	23±1	8.5	na	255	S	Y	S	(ECP)	CAPP, 2001
								Secondary Freshwater Data									
acute	vertebrate	fathead minnow	*Pimephales promelas*	7 days	survival	1,000	>1,000	>1,000	25	8	5.3-8.0	na	S	N	S	ECP	ERAC, 1998
acute	vertebrate	fathead minnow	*Pimephales promelas*	7 days	growth	500	1,000	>1,000	25	8	5.3-8.0	na	S	N	S	ECP	ERAC, 1998
acute	vertebrate	fathead minnow	*Pimephales promelas*	7 days	survival	500	1,000	788	25	>9	5.0-8.7	na	S	N	S	ECP	ERAC, 1998
acute	vertebrate	fathead minnow	*Pimephales promelas*	7 days	growth	500	1,000	>1,000	25	>9	5.0-8.7	na	S	N	S	ECP	ERAC, 1998
acute	invertebrate	daphnid	*Daphnia magna*	48 hours	survival	-	-	441	na	8	na	na	S	N	S	ECP	ERAC, 1998
acute	invertebrate	daphnid	*Daphnia magna*	48 hours	survival	-	-	289	na	>9	na	na	S	N	S	ECP	ERAC, 1998
chronic	invertebrate	daphnid	*Ceriodaphnia dubia*	7 days	survival	125	250	188	25	8	6.3-9.2	na	S	N	S	ECP	ERAC, 1998
chronic	invertebrate	daphnid	*Ceriodaphnia dubia*	7 days	reproduction	<31	31	164	25	8	6.3-9.2	na	S	N	S	ECP	ERAC, 1998
chronic	invertebrate	daphnid	*Ceriodaphnia dubia*	7 days	survival	125	250	180	25	>9	6.9-8.1	na	S	N	S	ECP	ERAC, 1998
chronic	invertebrate	daphnid	*Ceriodaphnia dubia*	7 days	reproduction	125	250	179	25	>9	6.9-8.1	na	S	N	S	ECP	ERAC, 1998
chronic	plant/alga	green alga	*Selenastrum capricornutum*	72 hours	growth	31	63	74	na	8	na	na	S	N	S	ECP	ERAC, 1998
chronic	plant/alga	green alga	*Selenastrum capricornutum*	72 hours	growth	7.8	16	63	na	>9	na	na	S	N	S	ECP	ERAC, 1998
								Unacceptable Freshwater Data									
acute	vertebrate	clawed toad	*Xenopus laevis*	48 hours	survival	-	-	410	na	na	na	na	na	na	na	na	De Zwart and Sloof, 1987
acute	vertebrate	goldfish	*Carassius auratus*	24 hours	survival	-	-	1,100	na	9.7	na	na	na	na	na	na	Bridie *et al* 1979b
acute	vertebrate	goldfish	*Carassius auratus*	24 hours	survival	-	-	>5,000	na	7.0	na	na	na	na	na	na	Bridie *et al* 1979b
acute	vertebrate	ide	*Leuciscus idus*	96 hours	survival	460	-	-	na	8.0	na	na	na	na	na	na	BASF AG, 1987a
acute	vertebrate	ide	*Leuciscus idus*	48 hours	survival	1,000	-	-	na	na	na	na	na	na	na	na	Huels AG, 1992
acute	vertebrate	mosquitofish	*Gambusia sp.*	48 hours	survival	-	-	1,350	na	na	na	na	na	na	na	na	Exxon, 1986
acute	vertebrate	mosquitofish	*Gambusia sp.*	96 hours	survival	-	-	1,350	na	na	na	na	na	na	na	na	Exxon, 1986
acute	vertebrate	stickleback	*na*	48 hours	survival	-	-	42	na	na	na	na	na	na	na	na	Exxon, 1986
acute	vertebrate	stickleback	*na*	96 hours	survival	-	-	42	na	na	na	na	na	na	na	na	Exxon, 1986
acute	invertebrate	daphnid	*Daphnia magna*	48 hours	survival	-	-	278	na	7.9	na	na	na	na	na	na	BASF AG, 1987b
acute	invertebrate	daphnid	*Daphnia magna*	24 hours	survival	-	-	354	na	7.9	na	na	na	na	na	na	BASF AG, 1987b
chronic	plant/alga	duckweed	*Lemna minor*	4-7 days	growth	-	-	1,500-2,300	na	na	na	na	na	na	na	na	SRC, 1994
chronic	plant/alga	green alga	*Scenedesmus suspicatus*	72 hours	survival	-	-	270	na	8.4	na	na	na	na	na	na	BASF AG, 1988
chronic	plant/alga	green alga	*Selenastrum capricornutum*	24 hours	^{14}C uptake	-	-	170	na	na	na	na	na	na	na	na	SRC, 1994
chronic	plant/alga	green alga	*Selenastrum capricornutum*	72-96 hours	biomass	-	-	7-30	na	na	na	na	na	na	na	na	SRC, 1994
chronic	other	cyanobacteria	*Aphanizomenaon flos-aquae*	24 hours	^{14}C uptake	-	-	130	na	na	na	na	na	na	na	na	SRC, 1994
chronic	other	cyanobacteria	*Aphanizomenaon flos-aquae*	24 hours	nitrogen fixation	-	-	150-200	na	na	na	na	na	na	na	na	SRC, 1994
chronic	other	diatom	*Cyclotella meneghiana*	24 hours	^{14}C uptake	-	-	110	na	na	na	na	na	na	na	na	SRC, 1994
								Unacceptable Marine Data									
acute	other	bacterium (microtox)	*Vibrio fischeni*	na	luminescence	-	-	50-60	na	na	na	na	na	na	na	na	SRC, 1994
acute	other	bacterium (microtox)	*Vibrio fischeni*	15 minutes	luminescence	-	-	9,202	na	8	na	na	na	na	na	na	ERAC, 1998
acute	other	bacterium (microtox)	*Vibrio fischeni*	15 minutes	luminescence	-	-	86	na	>9	na	na	na	na	na	na	ERAC, 1998

Notes:
General: - = no data or not applicable; na = not available.
Chemical Analysis?: Y = yes; N = no.
Controls Acceptable?: S = satisfactory; U = unsatisfactory.
Experimental Design: F = flow through; R = renewal; S = static.
Protocol: ECP = Environment Canada Protocol; (ECP) = Modified Environment Canada Protocol.

Table 2.6. Toxicity of Diisopropanolamine to Mammalian Species

Type of Study	Exposure Route	Mode of Administration	Carrier	Test Animal	Dosage	Units	Duration	Effect	Reference
Primary Data									
acute	oral	?	?	Rat	6,720	mg kg^{-1} bw	1 dose	LD_{50}	NIOSH UB6600000
acute	oral	?	?	Rat	5,660	mg kg^{-1} bw	1 dose	LD_{50}	Toropkov (1980b)
acute	oral	gavage?	water	Rat	3,980	mg kg^{-1} bw	1 dose	LD_{100}	Dow (1954)
acute	oral	gavage?	water	Rat	2,000	mg kg^{-1} bw	1 dose	LD_{0}	Dow (1954)
acute	oral	?	?	Mouse	2,120	mg kg^{-1} bw	1 dose	LD_{50}	Toropkov (1980b)
acute	oral	?	?	Guinea pig	2,800	mg kg^{-1} bw	1 dose	LD_{50}	Toropkov (1980b)
acute	oral	?	?	Rat	5,000	mg kg^{-1} bw day^{-1}	7 days	NOAEL	BIBRA (1991)
acute	oral	gavage	sunscreen	Rat (Albino)	5,000	mg kg^{-1} bw	1 dose	LD_{50}	Biosearch (1981a)
acute	oral	gavage	sunscreen	Rat (Sprague Dawley)	5,000	mg kg^{-1} bw	1 dose	NOAEL (mortality)	Springborn (1982a)
subchronic	oral	*ad libitum*	water	Rat (CFD Fischer 344)	3,000	mg kg^{-1} bw day^{-1}	2 weeks	2 of 5 males died, significant weight loss, reduction in body fat, organ sizes and weights, and altered clinical biochemical parameters, decrease in food and water consumption, acute inflammation and degeneration of kidney and urinary bladder, generalized liver atrophy	Dow (1984)
subchronic	oral	*ad libitum*	water	Rat (CFD Fischer 344)	1,200	mg kg^{-1} bw day^{-1}	2 weeks	Decrease in food and water consumption, weight loss in males, increased kidney weight relative to control, acute inflammation and degeneration of kidney and urinary bladder in only one animal (the other animals had no treatment related effects in the organs examined)	Dow (1984)
subchronic	oral	*ad libitum*	water	Rat (CFD Fischer 344)	600	mg kg^{-1} bw day^{-1}	2 weeks	NOAEL (activity, physical characteristics, gross pathology, organ weight, histology of liver, kidney, and urinary bladder)	Dow (1984)
subchronic	oral	?	?	Guinea pig	0.22	mg kg^{-1} bw day^{-1}	?	NOAEL (toxic effects)	Toropkov (1980b)
chronic	oral	*ad libitum*	food	Rat (Wistar)	391 ± 35	mg kg^{-1} bw day^{-1}	94 weeks	NOAEL (no carcinogenic effects in nasal cavity, lung oesophagus, liver, urinary bladder, or kidney)	Konishi *et al.* (1991) Yamamato *et a.* (1989)
chronic	oral	*ad libitum*	food (nitrite in drinking water)	Rat (Wistar)	448 ± 36 (DIPA) 151 ± 16 (nitrite)	mg kg^{-1} bw day^{-1}	94 weeks	Carcinogenic effects in nasal cavity, lung oesophagus, liver, urinary bladder, and kidney)	Yamamato *et al.* (1989)
Secondary Data									
acute	dermal	?	?	Rabbit	8,000	mg kg^{-1} bw	1 dose	LD_{50}	Union Carbide (1973)
Unacceptable Data									
acute	oral	?	?	Rat	0.055	mg kg^{-1} bw day^{-1}	7 days	NOAEL (reproductive effects)	BIBRA (1991)
acute	dermal	direct application to intact skin (abdomen)	undiluted DIPA	Rabbit	100	%	?	Moderate hyperemia to severe necrosis	Dow (1954)
acute	dermal	direct application to abraded skin (abdomen)	undiluted DIPA	Rabbit	100	%	?	Slight hyperemia, oedema, and moderate denaturation	Dow (1954)
acute	dermal	direct application to intact skin (ears)	water	Rabbit	10	%	?	NOAEL for dermal effects	Dow (1954)
acute	dermal	direct application to intact skin (abdomen)	water	Rabbit	10	%	?	Moderate hyperemia and blistering, oedema, and moderate denaturation	Dow (1954)
acute	dermal	direct application to abraded skin (abdomen)	water	Rabbit	10	%	?	Moderate hyperemia and blistering, oedema, and moderate denaturation	Dow (1954)
acute	dermal	direct application to skin	sunscreen	Rabbit (New Zealand)	1	%	1 dose (0.2 mL)	Mild primary irritation	Springborn (1982b)
acute	ocular	direct application to eye	undiluted DIPA	Rabbit	50	mg	1 dose	Burns on eyelid, eyeball and corneal mucosa	Toropkov (1980a)
acute	ocular	direct application to eye	sunscreen	Rabbit (Albino)	1	%	7 days	NOAEL (ocular irritation)	Biosearch (1981b)
acute	ocular	direct application to eye	sunscreen	Rabbit (Albino)	1	%	7 days	NOAEL (ocular irritation)	Springborn (1982c)
subchronic	oral	*ad libitum*	food	Rat (Wistar)	1	%	Age 6 to 24 weeks	NOAEL renal toxicity	Konishi *et al.* (1991)

? = *data not available in CAPP (2001).*

Table 3.1. Water Quality Guidelines for Diisopropanolamine

	Water Use				
	Freshwater Aquatic Life ***(mg L^{-1})***	***Marine Life*** ***(mg L^{-1})***	***Irrigation*** ***(mg L^{-1})***	***Livestock Watering*** ***(mg L^{-1})***	***Source Water for Drinking*** ***(mg L^{-1})***
Limiting Guideline	**1.6**	**-**	**3.9**	**38 (2)**	**21**
Guidelines	1.6	-	Loam: 91 (tame hay, cereal, pasture) 36 (other crops) Poor soil (1): 78 (tame hay, cereal, pasture) 3.9 (other crops)	38 (dairy cattle) 56 (beef cattle) 94 (deer)	21
Guideline Status	*Interim*	*Not Available*	*Interim*	*Preliminary (2)*	*n/a*

(1) The "poor soil" guideline is calculated using the species/endpoint/soil type combination that yielded the lowest guideline (see text). In practice, "poor soil" is either till or sand. The "poor soil" guideline is protective of plants growing in all soil types.

(2) Insufficient data to satisfy Protocol requirements for an Interim guideline. Guideline generated from mean LC_{50} value of 16 data points included in 3 studies using 4 routes of administration on 4 species of laboratory animals. Guideline is designated "Preliminary".